The American Journal of Obstetrics and Gynecology

VOL. XV ST. LOUIS, JANUARY, 1928 NO. 1

Original Communications

EPIDERMIDALIZATION OF THE CERVIX UTERI AND ITS RELATION TO MALIGNANCY

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FEW tissues of the body present such remarkable and varied reactions to pathologic stimuli as do the epithelial elements of the cervix uteri. Of prime importance among these are the processes which lead to a substitution of the cylindrical epithelium by a type of stratified squamous epithelium. These changes have been recognized for a long time but have received many interpretations and have been designated under a variety of names. The most descriptive of these is "epidermidalization" or, when the resultant tissue presents atypical characteristics, "epidermoidalization." Since the exact nature of the process is undetermined, the use of the term "metaplasia of cylindrical epithelium" and the incorrect interpretation of "stratification of cylindrical epithelium," which refers to a different change, should be discouraged.

EPIDERMIDALIZATION

The simplest way to describe this process is to regard it as representing a series of progressive changes by which the normal high cylindrical epithelium of the surface of the cervix uteri becomes substituted by a stratified squamous epithelium similar to that of the portio. In the first stage, there appears beneath the cylindrical cells and above the basement membrane of the mucosa a single row of new and distinctive cells (Fig. 1). These are small, polygonal in shape, stain deeply, and the nuclei are round or oval and somewhat large in

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proportion to the size of the cell. They are regularly arranged, and their general appearance at once suggests the basal-cell layer of stratified squamous epithelium. In the next phase, there is a proliferation of these infraepithelial cells until they form a stratified layer, varying from two to eight or more rows, which raise the cylindrical epithelium from its basement membrane (Fig. 2). (The resultant picture must not be confused with artefacts that may result from sections of cylindrical epithelium which have been cut obliquely and simulate a stratification of cells.) In this proliferation, there has been no change in the character of the individual cells. Mitotic figures are not seen.

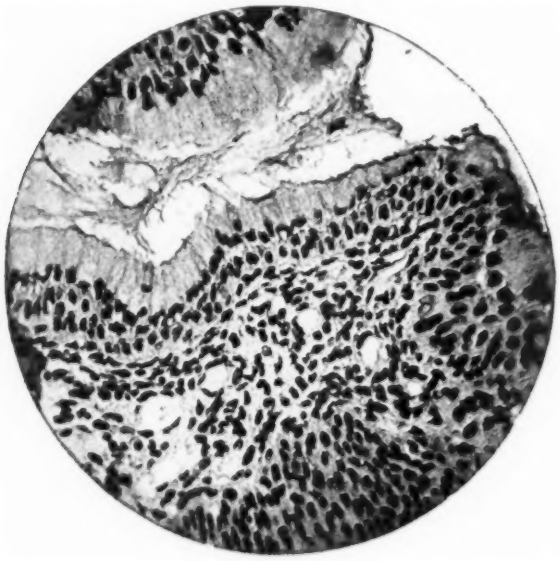

Fig. 1.—Epidermidalization. Single and double rows of small polygonal cells undermining normal cylindrical epithelium. (High power.)

The cylindrical epithelium has remained unchanged, but from now on it is deprived of proper nutrition, and there results a degeneration of its component cells so that they become completely cast off. The proliferating infraepithelial cells then undergo a process of differentiation (Fig. 3). The cells near the surface become larger, their outlines more distinct, the cytoplasm does not stain as deeply, and they assume a rectangular shape so that the resultant tissue is not unlike the transitional epithelium of the bladder and urethra. The lowermost cells, which represent the active proliferating portion, remain small and polygonal. The cells at the surface finally become longer and more flattened, and the differentiation progresses to the point where we find normal stratified squamous epithelium with its three distinct layers.

Epidermidalization occurs not only on free surfaces but also deep in glands, the proliferating cells rapidly extending beneath the cylindrical epithelium from one point to adjoining areas. Many extraordinary and unusual pictures may be presented by the various transitional phases. This is particularly true when the process occurs in glands, where the proliferating cells may form irregular masses which project into and even completely fill the lumen. At times certain cells capable of forming mucus become incorporated in the tissue, and as they become overdistended with secretion, small cavities, the contents of which show positive stains for mucin, appear among the layers of cells. There may also be a degeneration of some cells, resulting in small, partly necrotic areas. The resultant tissue then has a peculiar "fenestrated" appearance. This change has been designated by certain writers as a "mucoid degeneration," and Carl Ruge II[1] described a somewhat similar picture which he considered as a stratification of cylindrical cells occurring in infected cervical glands during pregnancy. Figs. 4 and 5 are sections of two glands from a mucous polyp of the cervix, showing various unusual forms which may be included under the term "epidermoidalization."

Fig. 2.—Later stage of epidermidalization. Stratification of infraepithelial cells. (High power.)

INCIDENCE

In order to determine the incidence of this phenomenon a study of 1280 slides, obtained from 1195 consecutive specimens of the cervix uteri, was undertaken. In this series a total of fifty-nine instances of

epidermidalization in various stages was noted, but in this number are not included thirty-five cases in which fully mature and normal squamous epithelium was found to be present within cervical glands. Figures for comparison could be obtained from only one source in the literature. Schottlaender[2] in 1912, in a study of 579 uteri, found these so-called metaplastic changes forty-seven times, thirty-three of which were in the cervix and fourteen in the body of the uterus.

An analysis of our fifty-nine specimens showed that in every instance there was a well-marked inflammatory process in the cervix. In fifty cases epidermidalization was occurring not only at the surface but also in the glands. Furthermore, in forty-one instances the pic-

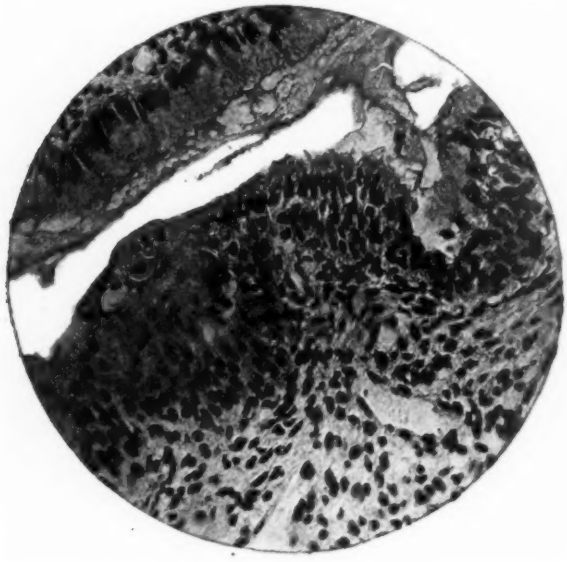

Fig. 3.—Epidermidalization. Transitional type of epithelium to left of picture. Undermined cylindrical epithelium on the right. (High power.)

ture presented was that of an erosion of the cervix in various stages of healing. It was thus apparent that in adults the phenomenon occurred as the result of a definite irritation in the form of an inflammatory reaction.

A few specimens of the cervix from newborn children were then obtained, and two of these definitely showed various transitional phases of epidermidalization in the cervical canal. This is in keeping with the work of R. Meyer[3] on pseudoerosio congenita, and Carl Ruge I.[4] in 1918, explained that the process of differentiation from cylindrical to stratified squamous epithelium on the portio was not completed at birth and that in many instances the various transitional phases could be demonstrated.

The most fertile field, however, was found in mucous polypi of the

cervix. In a previous study,[5] one hundred pathologic specimens of this condition were carefully analyzed, and in twenty-nine cases, epidermidalization was found occurring in localized areas on the surface of the polyp and involving the glandular elements. These areas most frequently were noted at the tip of the polyp when the base invariably showed normal cylindrical epithelium. Several of these specimens demonstrate very completely the whole process of epidermidalization in its various phases, and most of the illustrations for this article were obtained from sections of mucous polypi.

Although this paper is solely concerned with epidermidalization of the cervix, brief mention must be made here of the numerous refer-

Fig. 4.—"Epidermoidalization." Dilated gland in a cervical mucous polyp almost filled with atypical squamous epithelium, showing "mucoid" areas and areas of degeneration. (Low power.)

ences in the literature to a similar occurrence in the endometrium and in endometrial polypi. In this situation, it may present the various transitional stages described above (Herxheimer,[6] Sitzenfrey[7]). It has been found in the uterine body of a newborn infant (R. Meyer[8]) and of young children (Friedländer,[9] Hoehl,[10] Natanson[11]). In adults it is comparatively rare but has been described several times (Hengge,[12] Klein,[13] Sitzenfrey[7]). It has been associated with a pyometra (Bondi[14]), with tuberculosis of the uterus (Alterthum[15]), and with hyperplastic endometrium (Hunziker,[16] R. Meyer[17]), and Opitz,[18] and Herxheimer[6] have described epidermidalization on the surface of endometrial polypi projecting into the cervical canal. Finally, it has been found associated with adenocarcinoma of the body of the uterus,

and its relation to primary squamous cell carcinoma of the uterine body has been discussed by many authors (von Rosthorn,[19] E. Meyer,[20] Maunu af Heurlin,[21] Hitschmann,[22] Schauenstein[23]).

THEORIES

The simplest explanation for the origin of the infraepithelial cells, which play such a vital part in epidermidalization, is that they represent an ingrowth of basal-cells from adjacent normal squamous epithelium. Eichholz,[24] as a result of his researches on metaplasia, suggested that this was the most likely means of production. Frankl[25] is also in favor of this assumption, especially where we are concerned

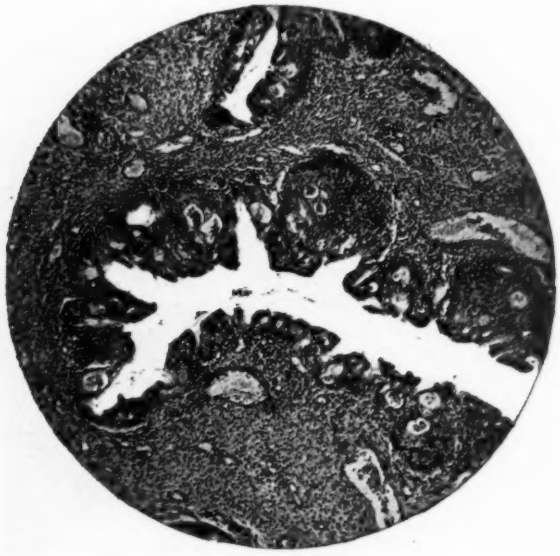

Fig. 5.—Gland in a cervical mucous polyp showing "epidermoidalization." (Low power.)

with the changes deep in the cervical glands, and R. Meyer,[26] in his theory of cervical erosions, gives this explanation for the process of healing.

The picture of normal stratified squamous epithelium growing into a cervical gland by direct extension and without a transitional stage is a very familiar finding, while in many instances of epidermidalization, a connection can be traced between the infraepithelial cells and the basal layer of adjacent squamous epithelium. It is thus very likely that we have here at least a frequent mechanism for the substitution of the cylindrical epithelium. However, it is insufficient to account for the occurrence of epidermidalization in three specific cases. It has been mentioned previously that squamous epithelium can often be found at the tip or lateral surfaces of a mucous polyp, when the

base of the polyp is totally covered by cylindrical epithelium and, therefore, no direct connection with the squamous epithelium can be established. Again, the occurrence of islands of epithelial cells showing epidermidalization and which are completely isolated has been frequently noted. Finally, the fact that it may occur primarily deep in a gland argues against the possibility of explaining epidermidalization solely on the basis of an ingrowth from adjoining tissues.

The work of R. Meyer[27, 3, 26] (Adair[28]) on the development of the epithelial covering of the cervix and his theory for the formation and healing of erosions is well known. He has shown that early in fetal life (third to fourth month) the undifferentiated cellular covering of the portio develops into squamous epithelium which extends high up into the cervical canal. At about the sixth month, cylindrical epithelium appears, which gradually forces the squamous epithelium out of the cervical canal. In this transition, a certain number of basal cells are left beneath the cylindrical epithelium, where they remain latent until some future time when under the influence of an external stimulus there is a weakening of the cylindrical epithelium. The rests of basal cells then begin to proliferate and result in a substitution of the cylindrical cells by a stratified squamous epithelium. According to R. Meyer, this accounts for the epidermidalization of polypi, healing of erosions, etc.

Are we concerned here with a metaplasia of cylindrical epithelium? The term has been frequently applied to these changes, but it is sometimes hard to determine if the word is used to imply simply a *substitution* and not a direct *conversion* of one tissue into another. The problem is whether the cells concerned in epidermidalization are derived directly from mature cylindrical epithelial cells. Considerable attention was devoted to this question by Kaufmann[29] and Oeri[30] in 1906, and they came to the conclusion that the infraepithelial cells concerned represented various transitional phases of a metaplastic process. However, many observers, notably Eichholz,[24] R. Meyer,[26, 27] Frankl,[25] Geller,[31] are very much opposed to the conception that this represents a true metaplasia.

It has also been suggested that there might be a direct implantation of squamous epithelium on a mucous polyp projecting from the external os and thus account for this type of epidermidalization. It is a possibility, but one which would be so limited by exceptions that, as R. Meyer[27] states, it is scarcely acceptable.

Another possible explanation, which has been mentioned, rests on the belief that certain embryonic undifferentiated cells may persist as inclusions in cylindrical epithelium. These units would contain in themselves the potentialities of developing into either type of tissue and would mature into squamous epithelium following a pathologic

stimulus, such as inflammation. Eichholz[24] and Geller[31] both mention this possibility. The theory, of course, requires for its support that the presence of such cellular inclusions be demonstrated. R. Meyer[3] found certain small cells occurring beneath the cylindrical epithelium, but in conformity with his theory, he considers them as representing rests of basal cells from squamous epithelium which previously covered that surface, and he does not see any reason for attributing a two-fold power of differentiation to them.[27] Krompecher,[32] as a result of his basal-cell studies, maintains that cylindrical epithelium has a basal-cell layer. These cells are of an embryonic character and may differentiate into a squamous epithelium. Such a process he would term dysplasia, or "regenerative dysplasia." Schmidt,[33] in a study of the regeneration of cylindrical epithelium of the cervix uteri, attached considerable importance to certain small round cells, with clear protoplasm, which are almost constantly seen among the cylindrical cells of the mucosa. He does not believe that they are wandering cells or leucocytes but that they are important factors in regeneration and are found in large numbers in rapidly growing polypi, erosions, etc. The problem is an interesting one and offers an attractive field for future work.

RELATION TO MALIGNANCY

The changes incident to epidermidalization have been studied for a very long time, and a review of the literature shows that various interpretations have been placed upon them, many of the older writers considering them as early malignancy. This is particularly true in regard to findings on cervical mucous polypi. In several cases these tumors were reported as showing early carcinomatous degeneration, notably by J. Williams,[34] Keitler,[35] Kroemer,[36] and Bulius.[37] The interpretation given by these writers has received considerable criticism from subsequent workers, who have maintained that insufficient evidence of malignancy has been brought forward and that it is more likely that they were concerned simply with epidermoidalization. Similar findings were described by Küstner,[38] Benthin,[39] Kaufmann,[29] and Oeri[30] and considered by them as representing purely benign conditions. In his book on *Cancer of the Uterus,* page 338, Cullen[40] gives an illustration, showing cylindrical epithelium both on the surface and within cervical glands undermined by cells, apparently an early phase of epidermidalization. He says, in regard to the finding, "I am entirely at a loss to explain just how this condition is produced, but have not the slightest hesitancy in saying that it is benign." Finally, more recent writers maintain that many cases of epidermoidalization are to be looked upon in the light of precancerous lesions (Stone,[41] Geller,[31] L'Esperance[42]).

It is very evident from what has been said regarding epidermidal-

ization that we are not concerned here with a malignant change. However, it is of vital importance to realize that atypical forms of the process may lead to confusion with carcinoma. Such confusion in the vast majority of instances will arise in those cases in which only a small biopsy specimen is available or where single sections have been cut at oblique angles and so yield a distorted picture. The error may occur in one of two ways: first, a specimen in which epidermidalization has resulted in an excessive proliferation of the cellular elements and the formation of atypical growths may present findings which at first sight very closely simulate malignancy; secondly, an early carcinoma or a section taken from the edge of a newgrowth

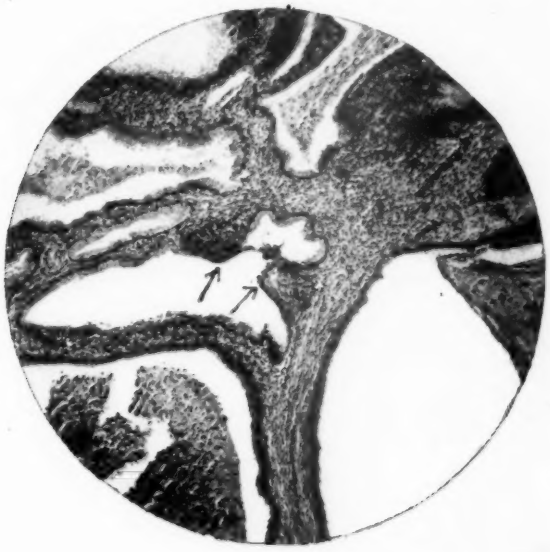

Fig. 6.—Cystic glands of the cervix uteri, one of which shows presence of cancer cells in two places. (Low power.)

may show such maturity of the constituent cells that it may be interpreted as epidermidalization.

In both instances the differential diagnosis is established by a very careful survey to ascertain the presence or absence of the so-called criteria of malignancy. These criteria have been enunciated by Schauenstein,[43] Pronai,[44] Rubin,[45] and Ewing,[46] and in this particular problem special attention must be paid to the following points of differentiation:

1. Atypical properties of individual cells. In carcinomatous tissue the cells present many irregularities; the cellular outline becomes indistinct while the protoplasm usually stains intensely; the nuclei are large, irregular, stain more deeply, show vacuolization and decay of nuclear substance, stand in no regular order with one another, and

are here and there gathered into clusters, and usually show atypical and asymmetrical mitotic figures.

2. Differentiation of tissue. It is here that epidermoidalization presents many difficulties. Although cancers of the cervix invariably show no regular stratification and are characterized by a richness in number of cells which lie closely pressed together, there are some slow-growing mature tumors which present fairly successful attempts to reproduce stratified squamous epithelium. Conversely, some cases of epidermidalization show masses of cells which have not assumed a regular stratified formation. Of considerable importance in this regard is a study of the basal-cell layers. In carcinoma the basal cells

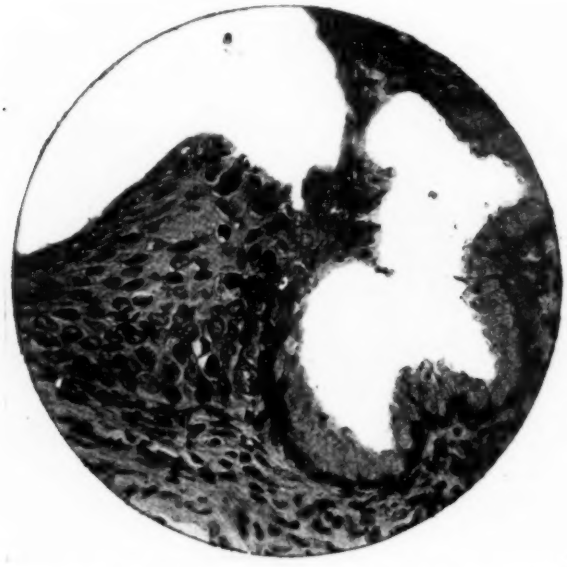

Fig. 7.—High power microphotograph of Fig. 6, showing cancer cells in wall of cervical gland.

invariably present an irregular arrangement and lie obliquely or transversely to the surface of the tissue, whereas in epidermidalization they more consistently lie in normal parallel lines.

3. Invasive and destructive properties of the proliferating cells. If at any point in a doubtful case definite invasion of the proliferating cells into surrounding tissue can be demonstrated, then there is no doubt that we are dealing with a malignant lesion. Schauenstein[43] has shown that cancer cells develop along the paths of least resistance, first extending along glands (Figs. 6, 7, 8) and then breaking out into adjoining tissues. If, however, no invasion can be demonstrated, we are still faced with the possibility of a very early carcinoma. In epidermidalization the cells are always limited to the glands, but artefacts due to sections cut across the fundus or sinuosities of a

gland may reproduce the picture of small nests of cells invading the surrounding tissues. Such findings must be carefully studied by serial sections in order exactly to determine their nature.

The finding of epithelial "pearls" has been considered a very valuable sign of malignancy, and Cullen[17] even states, "We have never seen an epithelial pearl in the squamous epithelium of the cervix except in cases of squamous cell cancer of this region." Although the demonstration of a pearl may be of some value in the question of diagnosis, its presence is not to be considered as pathognomonic for malignancy. Among the 1280 slides of the cervix that were studied in the

Fig. 8.—Cancer cells invading cervical gland. (Low power.)

preparation of this paper, four instances were found of epithelial pearls in normal or hypertrophied squamous epithelium occurring in specimens which showed inflammatory lesions and nothing suggesting a malignant change (Figs. 9 and 10).

In a masterly review of the subject of epidermidalization, R. Meyer[27] has called attention to another angle of the question, namely, that the stratified cells of epidermidalization must be differentiated from those occurring in a stratification of cylindrical epithelium. Although the latter may occur in inflammatory lesions of the cervix, it is much more marked and more frequent in carcinoma. The lower cell layers may be confused with the basal cells of squamous epithelium, although the latter are generally polygonal, while the proliferating cylindrical cells maintain their cylindrical form. In this connection, special stains to

demonstrate the presence or absence of mucin in the proliferating cells may be of considerable value.

Whenever sufficient tissue which has been properly sectioned at right angles to the mucous surface is obtainable, the differentiation between carcinoma and epidermidalization can invariably be made after a careful study. This has been the experience with the specimens available in the Stanford series, but a few of these show certain atypical formations, which, although they cannot be classified as definitely malignant, lead one to discuss whether they should be labelled with the term "precancerous." Here we are met with the problem of defining what is meant by "precancerous." A study of the literature shows that it is applied to a great variety of lesions of the cervix,

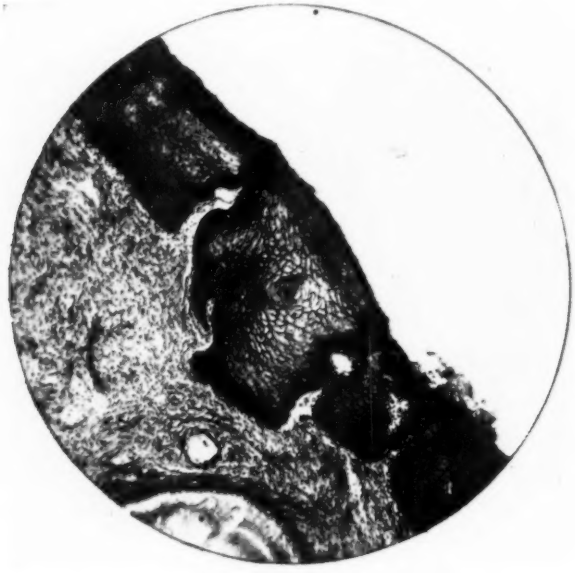

Fig. 9.—Epithelial "pearl" in noncancerous squamous epithelium of the cervix. (Low power.)

both clinical and pathologic. Since it has become generally accepted that chronic cervicitis is a frequent precursor of cancer, all severe inflammations of the cervix are often referred to as "precancerous," irrespective of the fact that in reality only a small percentage of these cases go on to malignancy. Ewing[16] states, "Precancerous diseases in themselves possess not a single essential element of the cancerous process," and L'Esperance,[42] "I believe that a precancerous lesion is only a potential carcinoma; some but not all go on to develop cancer."

From this standpoint many specimens showing epidermidalization could be considered as precancerous, because this lesion is so often found in connection with severe chronic inflammatory processes. But

here we are interested in the question from a more definite point of view. Cancer of the cervix develops from one or the other of its two epithelial tissues—cylindrical epithelium or stratified squamous epithelium. In epidermidalization, we find not only both these tissues but certain cells of a more immature type which represent a transition from one to the other. It is thus perfectly reasonable to assume that a cancer may develop from these elements. If this is so, is cancer more likely to develop from the cells of epidermidalization than from the normal epithelium of the cervix? Given two series of patients, one presenting evidence of epidermidalization and the other simply of chronic cervicitis, which will show a higher incidence of cancer? And finally, do those cases of epidermoidalization, where

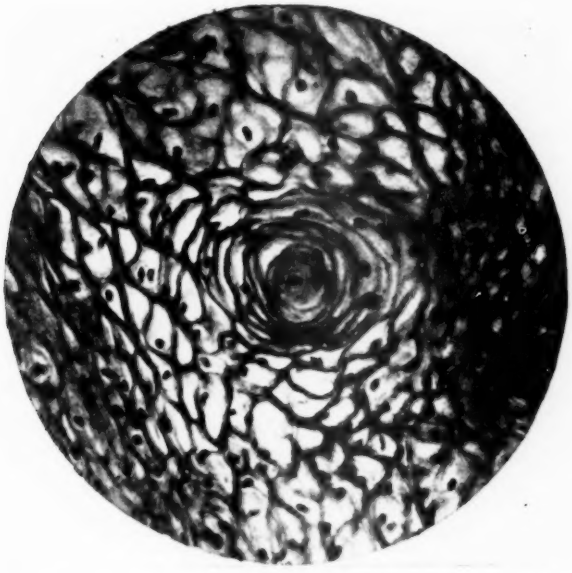

Fig. 10.—High power microphotograph of Fig. 9.

there is an excessive proliferation of the cells and the presence of atypical formation, necessarily represent a transition from a benign to a malignant condition?

Several authors are of the opinion that excessive proliferation of the cells concerned in epidermidalization may lead to carcinoma, and that at times this proliferation may actually represent a transition from a benign to a malignant condition. In 1906 Oeri[30] analyzed in detail a cervical mucous polyp showing epidermidalization, and although he considered it as representing a benign metaplastic process, he expressed his belief in the possibility of malignancy developing at a later date. Stone[41] in 1916 gave an excellent review of the subject of so-called precancerous conditions of the uterus and pointed out

that although the evidence was too scanty to confirm or deny the histogenetic relations between definite benign lesions and cancer, he was inclined to regard many of the findings of epidermidalization as representing phases in the transition towards a malignant growth. Geller[31] felt that they should be regarded as having malignant tendencies even if the histologic picture did not demonstrate this conclusively, because we are concerned with epithelial growths which have developed from undifferentiated cells after a long latent period, also because there is a disturbance of the normal tissue relations, and finally because there is nothing to assure us that the proliferation will in time come to a standstill. L'Esperance[42] believes that when epidermidalization occurs as the result of prolonged irritation, "it is in this relation to inflammation that it most frequently enters the picture of the precancerous process."

Considerable work has been done on this problem by R. Meyer,[27] who has studied with special care the patients who presented doubtful findings. Many of these have been closely watched, and in his opinion epidermoidalization in cases of hyperplasia and inflammation of the cervix is almost always benign. Ulesco-Stroganowa[48] believes that when atypical growths suggesting malignant hyperplasia are found in the cervix, the diagnosis of cancer is not justified if they can be explained as resulting from an active process, such as gonorrhea, erosions, syphilis, tuberculosis, etc. It is more logical to treat the primary condition and keep the patient under close observation than have her submit to an extensive operation. Frank[49] has called attention to the questionable diagnosis of "beginning cancer" in lesions which may as well turn out to be harmless epithelial proliferations, and the abuse of such conceptions which lead to radical operations solely "on suspicion."

The answer is difficult to find, for apparently no large series of patients who showed epidermidalization of the cervix and who did not have operative procedures has ever been systematically followed. None of the Stanford patients have ever returned with carcinoma of the cervix, but this evidence is of little value, as the material studied was obtained mostly from operative cases. However, the findings in mucous polypi are very suggestive, in that epidermidalization of these tumors is of frequent occurrence and malignancy comparatively rare. During the past fourteen years, only two cervical polypi showing carcinoma have been found at the Stanford Clinic. In only one of these is it certain that the change was in a definite, preexisting mucous polyp, and in both instances the cervix itself was involved. The incidence of epidermidalization, on the contrary, was found to be 29 per cent. Thus, it may be concluded that, at least as far as mucous polypi are concerned, epidermidalization seldom if ever leads to a malignant degeneration.

On the whole, epidermidalization is a purely benign local tissue reaction. At times it may lead to the formation of atypical growths which may be confused with an early carcinoma. A careful study of serial sections and repeated biopsies will invariably clear up the diagnosis. Very rarely cases are met with in which it is impossible to determine whether we are dealing with a benign hyperplasia or an early malignant change. These may be labelled "precancerous" and treated accordingly, but it is probable that the majority of even these will eventually prove harmless.

SUMMARY

By epidermidalization is meant a process by which the normal cylindrical epithelium of the cervix is replaced by a stratified squamous epithelium. Five theories have been suggested to account for the exact mechanism involved in this change. It was found to occur in fifty-nine instances of chronic cervicitis from a series of 1195 specimens of the cervix and in twenty-nine of 100 cervical mucous polypi. It was also noted in newborn cervices, and there are many references in the literature to the finding of squamous epithelium in the endometrium.

At times the process may lead to the formation of atypical epithelial overgrowths, which may be termed "epidermoidalization." Careful study of serial sections and repeated biopsies may be necessary to differentiate these findings from an early carcinoma. In rare instances, malignancy can be excluded, but certain features are present which may be considered as "precancerous." It is not certain that these really represent transitions from a benign to a malignant growth, and there is reason to believe that most of them would probably prove to be harmless.

Due acknowledgment is made to Mr. Pierre Lassègues for the microphotographs used in this article.

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A NEW OBSTETRIC FORCEPS*

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THE anticipation of trouble during labor by the careful examination of patients during their pregnancies and at the onset of labor and the improvement of the technic of cesarean section has greatly reduced the incidence of difficult forceps operations. Though it is known that the amniotic sac becomes infected very soon after the rupture of the membranes, whether vaginal examinations have been made or not, the perfection of the low cesarean section by Beck, DeLee, Latzko, and others has decreased the dangers of peritonitis so much that in borderline cases long trial labors can now be advised, resorting to one of these operations should failure occur. There is no question that the cesarean section is indicated when there is any bony obstruction and craniotomy, if the child has been seriously compromised. We are no longer justified in attempting difficult operations through the birth canal in such cases, when the high infant mortality and the injury to the mother are considered.

The actual misjudging of the size of the baby and pelvis, though it occasionally happens, does not play a large part in difficult labors. A greater proportion of these are caused by the malpositions of the

*The completed instrument herewith described was first presented at a meeting of the New York Obstetrical Society, November 10, 1925.

child's head due to torsion or rotation of the uterus which are so frequently found in deformed pelves. The woman can usually overcome a moderate bony obstruction by her own forces and the resultant molding of the head, provided the head can be fitted squarely into the axis of the pelvis. This frequently can be done by binders and by changing the position of the patient during labor. If the presenting part does not adapt itself to the inlet, allowing the head to act as a ball valve, early rupture of the membranes is common with a

Fig. 1.—Barton forceps assembled.

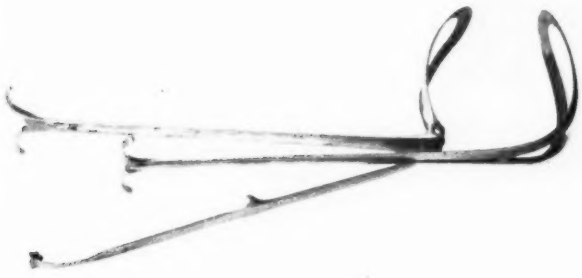

Fig. 2.—Farabeuf cephalometer.

resultant long and difficult labor. The use of the De Ribes or Voorhees bag is often necessary to complete the dilatation of the cervix. After dilatation of the cervix, combined manipulations from above and below permit correction of the malposition, though failure to do this has occurred earlier in labor. Unfortunately, secondary uterine inertia frequently occurs with the head still high in the pelvis and above the brim. Under such condition, with no bony obstruction and with the soft parts out of the way, version or forceps can be resorted to rather than cesarean section. It is in such cases that the Barton

forceps are frequently of great use. The mortality for the mother in cesarean section is still so high that we feel that a thorough study of the mechanism of labor is of value.

While at the present time, there are a number of different types of obstetric forceps which may be successfully employed in low forceps and midforceps operations, no one of them, however, in high forceps operations is equally efficient. This is due to the fact that the forms of the various forceps, as now constructed, render them not equally well adapted to both the head and the pelvic axis except in the low positions and necessitate, in the high forceps operation, the adoption of either the pelvic or cephalic methods of application. As a result of this lack of simultaneous adaptability in the pelvic method of ap-

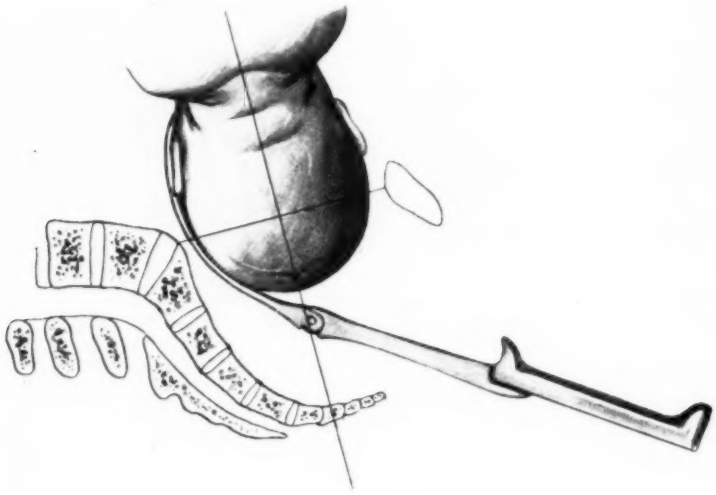

Fig. 3.—Introduction of anterior blade in midline posteriorly.

plication, the relation between the forceps and the head is faulty; in the cephalic application, the relation between the forceps and the pelvic axis is faulty.

With both the pelvic and cephalic methods of application, certain unfavorable conditions are associated, which may be stated as follows:

In the pelvic application, the grasp of the head by the blades is either over the face and the occiput, or over one brow and the opposite mastoid region, according to where the occipitofrontal diameter of the head lies in the transverse or oblique diameters of the pelvis and, as the cephalic curve of the blades is not well adapted to the surfaces with which they are in apposition, difficulty is experienced in locking the forceps; during traction, if the head becomes slightly extended, the blades are liable to slip; the line of traction is not coincident with the axis of the superior strait; normal rotation during descent is interfered with, and the compression of the head by the blades is in the least favorable diameter and is often followed by intracranial hemorrhage.

In the cephalic application, while the blades may be accurately applied over

the parietal bones, the long axis of the forceps is not coincident with the axis of the superior strait and results in a faulty line of traction; the head is tilted laterally toward the pubes, relatively increasing the size of the head in excess of the biparietal diameter (Figs. 8 and 9); during descent, the posterior blade bridges over the hollow of the sacrum and interferes with the entrance of the head into the pelvis.

In addition, many forceps have widely diverging blades in advance of the head which, unless great care is exercised, are the starting point of the serious lacerations. It should be evident, therefore, that it is not possible to apply any forceps, whose blades are parallel with the shanks, by either the pelvic or cephalic methods, but that the result will be a disturbance of the normal relation of the head to the pelvic

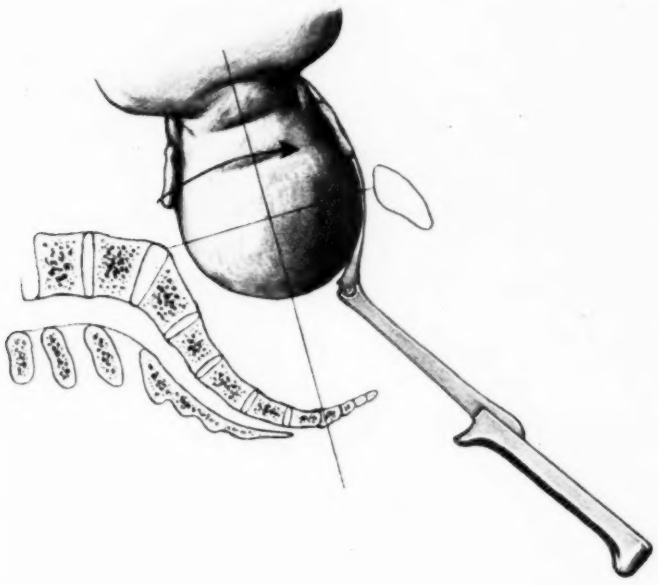

Fig. 4.—Anterior blade rotated to position in front of head.

axis by either a rotatory or lateral displacement, bringing longer diameters of the head in conjunction with shorter diameters of the pelvis, increasing the amount of traction force necessary to effect delivery and also the risk of undue compression of the head and injury to the structures of the parturient canal.

It is necessary, therefore, that forceps designed to avoid the above-mentioned conditions should possess certain qualifications, namely, their form should be such that they are adaptable to both head and pelvic axis at the same time, permitting a cephalic application without disturbing the normal relation of the head to the pelvis; they should have no widely diverging blades in advance of the head; they should, in no way, interfere with the normal mechanism of labor. The Barton forceps was designed to comply with these qualifications.

DESCRIPTION OF FORCEPS

These forceps differ from the usual types in that the blades join the shanks at an angle, as shown in Fig. 1. This angle is the normal angle between the axis of the superior strait of the pelvis and the axis of the pelvic outlet. This construction permits an accurate cephalic application, in cases of arrest of the head at the pelvic brim, in either the transverse or an oblique diameter, without disturbing the normal relation of the head to the pelvic axis.

Owing to the peculiar shape of the anterior blade, for the purpose of application, it is necessary to incorporate a joint at the junction of the blade and shank. By means of this joint, the blade can be swung through an arc of a circle until it is nearly parallel with the shank, as shown in Figs. 3 and 4.

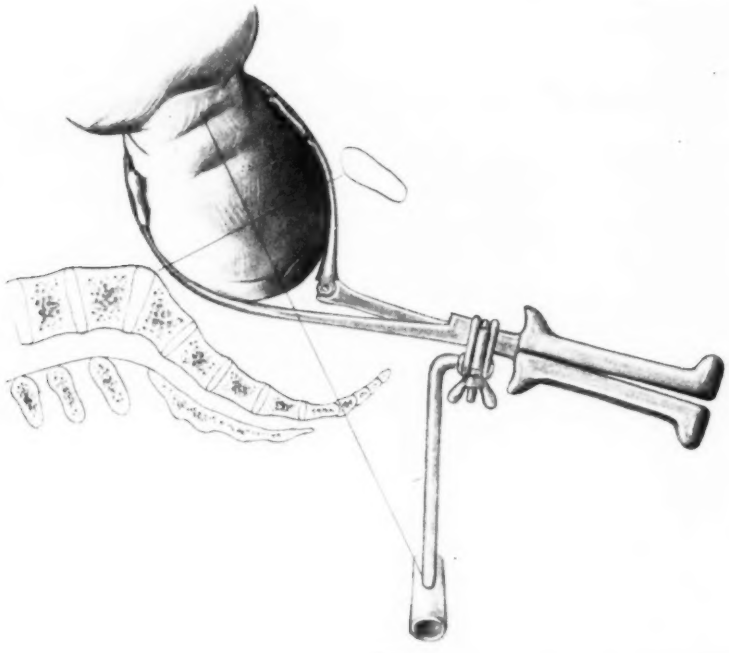

Fig. 5.—Posterior blade introduced, forceps locked, axis-traction rod attached. Note normal relation of head to pelvic axis and handle of axis-traction attachment in line with the axis of the superior strait.

The lock of the forceps is so constructed that a gliding motion of one member on the other is permitted; this insures the adaptability of the blades to heads of varying sizes without destroying the symmetry of the space between the blades.

The axis-traction attachment consists of the customary cross-bar handle pivoted on the end of the traction rod. The other extremity of the traction rod is pivoted to the yoke which partially encircles the shanks of the forceps. On one side of the yoke is a lug through which passes a tension bolt, the horizontal portion of the tension bolt lying in vertical slots on each side of the yoke. (Fig. 5.)

To apply the axis-traction attachment to the forceps, loosen the winged nut sufficiently to permit the tension bolt to be raised from the vertical slots and rotated ninety degrees. Apply the yoke to the forceps shanks from below, rotate tension bolt to proper position for its horizontal portion to enter the vertical slots, and tighten the winged nut.

In order to apply and manipulate the Barton forceps properly certain conditions are essential; namely, an exact cephalic application should be made, as is determined by having the sagittal suture midway between the heels of the blades; the position of the shanks and handles in the vertical plane should be such that the axis of the blades is coincident with the pelvic axis; rotatory displacement of the head should be corrected by rotating the forceps on its long axis, to either right or left as required, in conjunction with a lateral movement of the handles in the horizontal plane in a corresponding direction; the relation of the blades to the head should be such that, during descent, flexion is encouraged and not antagonized; direct traction in a line with the shanks and handles should never be employed, but instead, a modified Pajot maneuver.

Dr. Barton got the idea of his instrument from observing that dentists used a different type of extracting forceps for the molars than for the incisors. He believed that we were attempting deliveries in

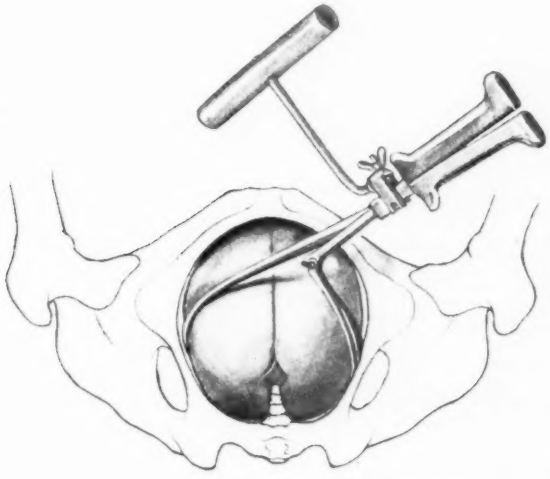

Fig. 6.—Rotation of head completed.

the upper pelvis with forceps which were designed for the lower pelvis and which could only be used to best advantage at this point. With the idea that there should be an entirely different principle in forceps intended for high application, especially in transverse and occiput posterior positions, he designed the instrument described in this article. Farabeuf had developed a similar instrument but only for the purpose of measuring the fetal head. Apparently, the possibility of such an instrument as a forceps did not occur to him. (Fig. 2.)

Dr. Barton made the first drawing of this forceps more than twenty years ago. It was not until the first model was made in 1923 that attention was attracted to the possibilities of such an instrument. Experience with the Barton forceps has shown that the first model constructed had too wide an angle between the blades and the blades were too short, especially when applied to heads above the normal in

size. This led frequently to slipping of the forceps and may account for some of the failures reported in the appended case histories. Unfortunately, this is the model owned by a majority of men using this instrument. In the present model this defect has been corrected by lessening the angles between the blades and by increasing their length.

It takes considerable time and practice on the manikin to realize that it is not a traction instrument but rather one for leverage and rotation. The direction of the pelvic axis and the relation of the forceps to this axis must always be borne in mind. When the forceps are ap-

Fig. 7.—Delivery by extension of the head.

plied, at the brim or above, the sagittal suture must be directed backward toward the hollow of the sacrum before any attempt at traction is made. If the sagittal suture is directed downward or anteriorly, asynclitism results, with slipping of the blades and failure of the forceps. The anterior blade is of great use and is easily applied in helping to correct anterior or posterior parietal presentation. Its function in this instance is merely as a lever. Both blades can be used in helping in the rotation of a persistent occiput posterior in the hollow of the sacrum. We have found it more useful in these cases than any other forceps with which we are acquainted. Failure is common, and birth injuries result when attempts are made to rotate the head before the biparietal diameter has come through the pelvic brim.

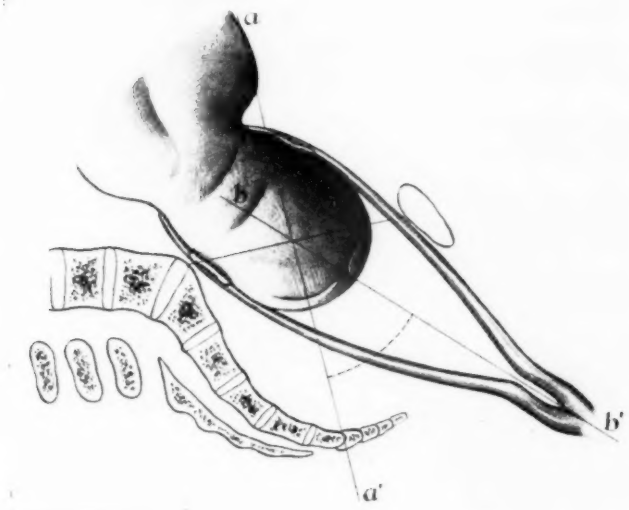

Fig. 8.—Cephalic application of the Tarnier forceps. Note lateral tilting of the head and faulty line of traction as represented by the angles formed by the lines aa^1 and bb^1.

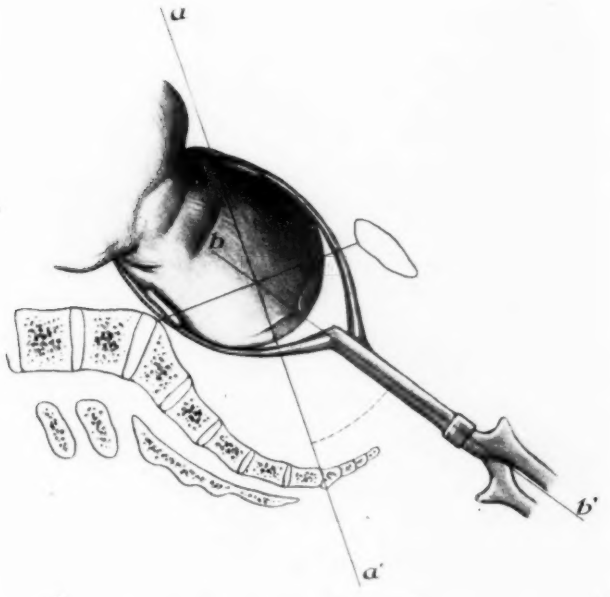

Fig. 9.—Cephalic application of the Kielland forceps. Note the lateral tilting of the head and faulty line of traction as represented by the angles formed by the lines aa^1 and bb^1.

It is surprising how far down the head has to be pulled before this is accomplished and rotation can be attempted. With marked molding and a large caput succedaneum, it is often necessary to bring the head almost to the pelvic floor.

If the Barton forceps are to be used at the outlet after rotation, it is important to see that the shank of the forceps lies in a line perpendicular to the posterior fontanelle. Otherwise, slipping of the forceps with extension of the head and a consequent birth injury may occur. After rotating the head, the application of the ordinary type of forceps to complete the delivery is often the easiest maneuver.

During a period beginning November 23, 1924, and ending May 31, 1927, the Barton forceps have been used in forty-eight cases at Sloane Hospital for Women by thirteen operators. Of these cases fourteen have been classified as high, and thirty-four as medium forceps operations.

The cases in the first group showed an average labor of thirty hours before forceps were applied. Dry labor occurred six times. The pelvis was normal in six instances, simple flat in three, generally contracted in three, and in two cases there was a long symphysis with a poor inclination. Complete delivery was accomplished by Barton forceps in three instances. In the other cases some other type of forceps was applied after the head had been brought down to the floor and rotated by means of Barton forceps. No extensive laceration occurred. In four instances bad fetal results render the brief summarization of these cases worth while.

CASE 1.—7264. Para 0; gravida 1. Generally contracted pelvis with diagonal conjugate of 11.5 cm. Dry labor with duration of forty-four hours. Pains poor in quality. Bag used to dilate cervix. Barton forceps applied but failed to advance head. Forceful delivery by Simpson forceps and axistraction. Stillbirth. Autopsy showed a lacerated tentorium and congenital pneumonia. Note on chart recommends cesarean section at next delivery because of bony disproportion.

CASE 2.—No. 6830. Para 0; gravida 1. Flat pelvis with diagonal conjugate of 11 cm. Duration of labor fifty hours with poor inefficient contractions. Head L. O. T. at brim. Barton forceps applied. Delivery accomplished with difficulty. Stillbirth. Autopsy showed laceration of tentorium.

This patient delivered normally in March, 1927.

CASE 3.—No. 6111. Para 3; gravida 4. Normal pelvis. Details of labor not noted. Head in R. O. T. at brim. Difficult delivery. Large baby; shoulders impacted. Died during reduction of latter. No autopsy.

CASE 4.—No. 8124. Para 0; gravida 1. Pelvis with long symphysis and poor inclination. Dry labor with a duration of twenty hours. Head R. O. T. at brim. Barton forceps applied but failed to advance head. Version and breech delivery. Stillbirth. No autopsy.

Only in Case 2 (No. 6830) can the bad result be attributed to the use of Barton forceps alone. Other factors are concerned in the remaining three.

The average duration of labor in the cases delivered by medium

forceps operation was twenty-three hours. Dry labor occurred fourteen times. The pelvis was normal in fifteen instances; in eleven cases a long symphysis with poor inclination was noted; of the remainder, five were generally contracted, three were simple flat, and one was a rachitic flat type. In sixteen cases the head was in the occiput posterior, in eighteen cases in the occiput transverse position when the forceps were applied. In eleven cases the complete delivery was accomplished with these forceps. In the remaining cases some other type of forceps was applied after the head had been brought down to the floor and rotated. No extensive lacerations were caused. Five cases are summarized below because of bad results, some of which are not due solely to the use of these forceps.

Case 1.—No. 6573. Para 0; gravida 1. Flat pelvis with diagonal conjugate of 11 cm. In labor forty-nine hours with infrequent, inefficient pains. Barton forceps applied in midpelvis with head in L. O. T. Head brought down and rotated. Delivery completed with Simpson forceps. Baby in poor condition. Died second day. (Death may have been due to congenital pneumonia.) No autopsy. This patient had subsequent normal delivery.

Case 2.—No. 7694. Para 0; gravida 1. Pelvis had long symphysis with poor inclination. Dry labor with irregular inefficient contractions. Duration twenty-seven hours. Barton forceps applied to head in R. O. P. in midpelvis. Unable to advance head. Delivery finally accomplished with Milne-Murray forceps.

Case 3.—No. 9311. Para 0; gravida 1. Pelvis generally contracted with diagonal conjugate of 11 cm. Duration of labor thirty-seven hours. Fetal heart slowed so Barton forceps were applied to head in R. O. T. Complete delivery accomplished. Stillbirth. Autopsy showed bilateral tear of the tentorium.

Case 4.—No. 9381. Para 0; gravida 1. Normal pelvis. Duration of labor not noted. Barton forceps applied to head in high midpelvis. No advance of head. Forceps were removed. Fetal heart had been good but now could not be obtained. Forceps reapplied and rapid forceful delivery was made. Stillbirth. No autopsy.

Case 5.—No. 9702. Para 0; gravida 1. Normal pelvis. Duration of labor seventeen hours, a large portion of which was dry; weak contractions. Barton forceps applied to head in R. O. T. in midpelvis. Head brought to floor and rotated. Delivery completed with Milne-Murray forceps. Baby died on seventh day. Autopsy showed laceration of the tentorium.

In addition to the above cases Dr. Caldwell has delivered eighteen cases at other institutions by means of the Barton forceps, of which details are not available. Stillbirths occurred in four instances. In two cases the fetuses were macerated, in the remaining two the presence of the fetal heart was doubtful before the forceps were applied.

Dr. Barton and his associates have used the forceps in twenty-five cases in practice at Plattsburg, New York, and vicinity. All of these have terminated successfully for mother and child except in one instance, in which an eclamptic was delivered of a premature stillbirth.

There has been no maternal mortality and but one serious laceration in the entire series of cases.

CONCLUSIONS

1. The Barton forceps allow an easy cephalic application in the axis of the birth canal, especially when the head is high in the pelvis.

2. The Barton forceps can be easily used to help correct malpositions of the presenting part.

3. The axis of the pelvis in its relation to the position of the child's head must at all times be considered.

4. The extraction of the child is by a leverage or modified Pajot's maneuver rather than by direct traction.

5. Cases in which these forceps are useful require careful study by a skilled obstetrician. They have a definite value in his hands.

6. They will not overcome bony obstruction. They will not overcome obstruction due to soft parts without injury to both mother and baby.

THE PRESENT STATUS OF THERAPY OF CANCER OF THE UTERUS*

By John Osborn Polak, M.D., F.A.C.S., Brooklyn, N. Y.

WHEN your President drafted me to speak at this, the opening meeting of his administration, I was at a loss as to the selection of a topic, for as we review the literature we cannot help but be impressed with the fact that the diagnosis and treatment of most of the conditions peculiar to women are accepted and standardized. This is apparently not so in the therapy of cancer of the uterus, for from the clinical reports which are constantly appearing, the superiority of the radical operation versus radium and x-ray still appears to be a subject of contention. For instance, Bonney, in a recent publication in which he reports 214 radical operations done at the Middlesex and Chelsea Hospitals for Women, proclaims the superiority of surgery; and Weibel with his immense mass of material and his high incidence of operability, claims results which have never been equaled in this country; i.e., 87 per cent cures in incipient cases,—53 per cent in the mild and 28 per cent in the severe type. On the other hand, Heyman, Foershil, Döderlein and others champion the value of radium and perhaps justly so, for the primary operative mortality of the radical operation ranges from 5 to 42 per cent. It is therefore in an effort to give a summary of the present status of cancer therapy that I shall take up the discussion.

It may be said that definite progress has been made in the cancer situation, first, in the classification of the degree of malignancy, for

*Read at a meeting of the Brooklyn Gynecological Society, March 4, 1927.

serial sections of the specimens removed have shown that certain groupings and forms of cells are more malignant than others and all pathologists are agreed that the spindle-celled cancer is the least malignant. Though these facts have been definitely settled, it has not been determined whether this form of cell is more amenable to surgery than to radium. All of this study has, however, demonstrated the necessity of cooperation between the pathologist and the clinician, and proves that our cancer slogan must be *early diagnosis* and *intensive treatment*.

A second step in progress has been a better appreciation of the routes of extension, for this has made it possible to limit the lymphatic advance in cervical cancer by the production of lymphatic block. Lymphatic block may be accomplished either by surgery or by the x-ray. Furthermore, the accepted recognition of the fact that *only one group of cases*, that is, those which are classed as Group I, *where the growth is wholly within the confines of the cervix*, are amenable to surgical extirpation, is a great step in advance, for the acceptance of this principle will save many lives and prolong the life of many others. *This means that all borderline cases fall within the range of radium* and not operation. Nothing spreads cancer so quickly as the manipulation of cancerous tissue, such as occurs when an incomplete extirpation is made through malignant structures.

In a collective review on this subject, which I published a year or so ago, I called attention to the high operative mortality of radical extirpation of the uterus for cancer of the cervix, and then stated that all experimental study has shown that the cancer patient produces an immunity of varying degree to the extension of any malignant growth. This is evidenced by the surrounding cellular infiltration, the glandular enlargement, and the glucose consumption. Anything which breaks down this resistance, such as blood loss, tissue trauma or metastatic extension through manipulation, or change in the sugar content of the blood as produced by anesthesia, favors extension.

In support of these clinical observations, the result of postoperative studies has shown that at every operation in which the abdomen is opened, which entails the use of general surgical anesthesia, there is reduction in the blood sugar and in the carbon-dioxide combining-power, together with blood loss and tissue trauma. These are constant factors which are met with and must be combated.

These clinical findings are supported by the experiments conducted by the late Doctor Harvey Gaylord, who, while in charge of the New York Institute for the Study of Cancer, made a series of experiments on rats with implanted malignant growths. Gaylord found that he could implant cancer in a healthy rat, feed the rat properly and give it limited freedom; in other words, if he could keep up the rat's natural resistance, the rat established an immunity against the growth which would

remain stationary for periods of three to five years. When, however, he began giving these rats general anesthetics, he was surprised to find that there was an immediate extension of the growth which had lain so long dormant. This we know was probably due to the effect of the anesthetic on the sugar content of the blood and to the lowered carbon-dioxide combining-power, both of which reduced the individual resistance.

The second experiment consisted in bruising the tissues which immediately surrounded the graft; this again led to rapid extension.

Having demonstrated that an implanted growth would remain dormant unless the contiguous tissue was traumatized and the immediate protective barrier broken down by the lack of sugar content, he began to study the effect of anemia on the development of implanted growths. He, therefore, began by drawing off one or two drops of blood each day from the rat's tail. When he had produced a moderate secondary anemia, he found that the cancer implant grew very rapidly.

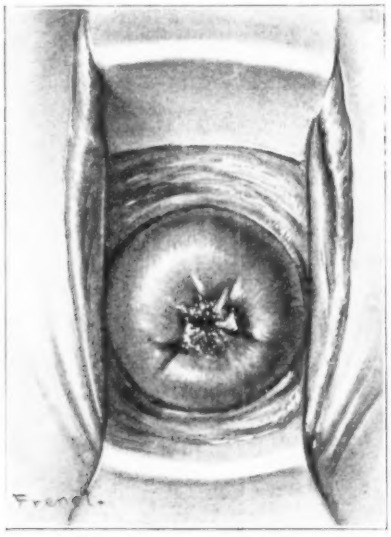

Fig. 1.—Cervical epithelioma, inverting type.

In view of these experiments it seems apparent and in line with the clinical experience of every operator, i.e., that these basic conditions obtain at every operation and that, unless the entire growth is removed and the surrounding glands extirpated, operation hastens rather than defers the final termination by supplying the three factors that have been referred to in these experiments.

Cancer of the cervix may begin as a nodule on the portio, in the cervical canal, or in the cervical glands. When it has its origin on the portio or in the columnar epithelium of the cervical canal, it appears as an epitheliomatous growth; while when its origin is in the cells lining the glands of the cervix, it takes on the form of an adenocarcinoma. Clinically, the growth may assume an inverting or everting character. It is in the latter that the earliest subjective symptoms

appear. Whatever its origin and whatever its cause, the earliest subjective symptom of cervical cancer is some form of anomalous bleeding. This bleeding does not appear until tissue necrosis has occurred, hence while hemorrhage is the earliest symptom, the growth in the inverting type may have advanced to a considerable extent before this sign is manifest. This explains why so many cases pass unrecognized in their incipiency; for it is not until we treat every suspicious ulceration and bleeding as a potential cancer and have the cooperation of a competent laboratory, that we may hope to make great advance in the early diagnosis. Even in Austria, where cancer propaganda has been carried into every home, only 6.5 per cent come to the surgeon in the incipient stage.

Fig. 2.—Section through cervix showing extension in inverting type with an innocent looking external os.

Cervical erosion is a constant precursor of cancer, while extreme cervical laceration with ectropion supplies another source of chronic irritation. Therefore, we can appreciate what a heavy responsibility is placed upon the practitioner in the treatment of cervical lesions resulting from laceration or infection. The preventive treatment of cervix cancer will hinge upon the differential diagnosis of these conditions and their proper treatment.

Some years ago, Hofmeir called attention to the fact that a simple ulceration or an erosion was coated with a mucoid discharge, while malignancy always changes the character of the discharge; and that if a 10 per cent solution of copper sulphate was applied to the sur-

face of a simple erosion or ectropion a resulting white eschar would form upon it, while if it were a cancerous ulcer the copper sulphate solution would cause it to bleed. For many years this suggestion and the friability of cancerous tissue have aided us in making the early diagnosis. However, we do not depend on this or on any other physical appearance, but subject the cervix in every suspicious case to histologic study.

Just a word as to taking biopsy specimens. The section should be removed with a very sharp, thin-bladed knife *and the wound immediately sealed with the actual cautery*, for all experience shows that curetting or removal of a specimen with a tonsil punch is apt to cause

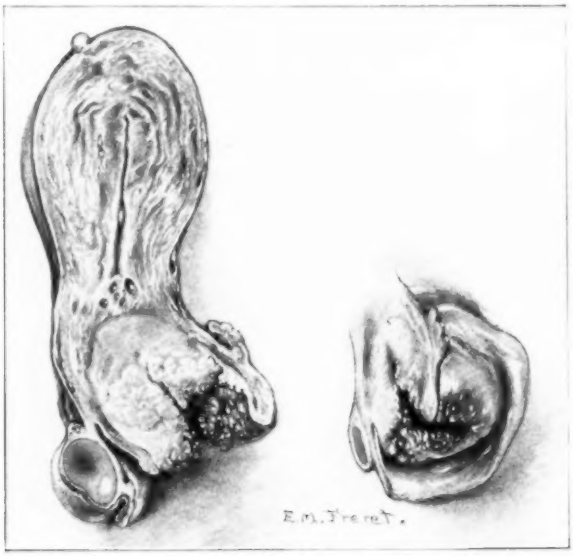

Fig. 3.—Everting type. Extension along contiguous vaginal mucosa.

metastatic extension just as vigorous or repeated bimanual manipulation will do the same thing. Cancerous tissue *must be* handled gently.

Remember that every failure to make a diagnosis of incipient cancer costs a human life; therefore, it is better and less harmful to take ten unnecessary biopsy specimens than to miss one in which the disease has actually developed.

The preventive treatment of cancer is what should occupy us at the present time. This means the cure of endocervicitis, cervical erosions, and the repair of lacerations, or the amputation of extensively diseased cervices which are found in women during the third decade of life.

When cervical cancer is recognized, the question that must be settled at once, before the selection of any form of radical treatment is

instituted is, within what group does the cancer fall? Group I implies an ulcer or nodule on or in the cervix surrounded by an immediate area of infiltration. The tissue bleeds on manipulation or on the application of a tenaculum. There must be no extension into the parametria or into the adjacent vaginal wall. Rectoabdominal examination of both broad ligaments and of the uterosacrals will demonstrate this point. Bimanual examination of the fornices will exclude any extension along the mucous membrane or into the uterovesical tissues. *Only this class, where the growth lies wholly within the confines of the cervix, having free mobility, should be considered for radical surgical extirpation.*

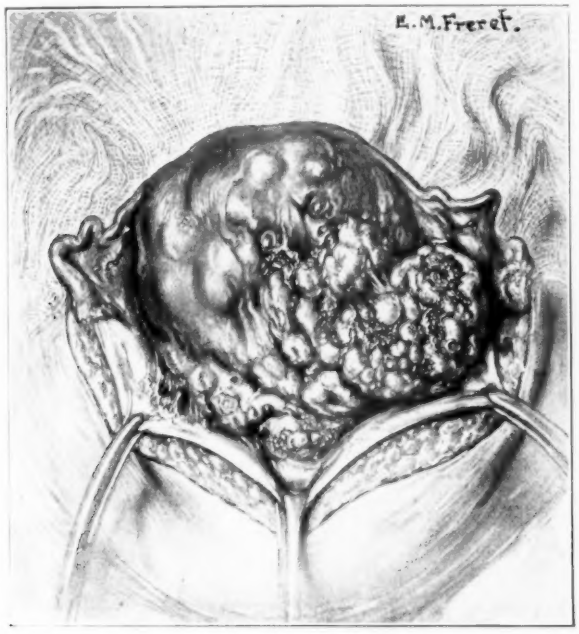

Fig. 4.—Extension of a corporal cancer through the uterine wall.

The so-called Wertheim operation or radical extirpation which includes removal of tubes, ovaries, parametria, vaginal cuff and contiguous iliac and sacral glands, carries with it an operative mortality of from 5 to 42 per cent.

Bonney's report of 214 consecutive cases showed 34 deaths directly attributable to the operation. Weibel, whose vast experience has permitted a perfection of technic, has a 3 to 10 per cent primary mortality, and the end-results after five years run from 87 per cent (Weibel) to 33 per cent (Clarke) in incipient cases. About 50 per cent of the primary fatalities are from septic peritonitis.

When we compare these figures with those obtained from radium

after the five- and seven-year period with no operative mortality, such as the results reported by Haymen and Forsell who with a 100 per cent follow-up have 59 per cent of cures, or those of Ward with 52 per cent and those of Bailey and Healy with 51 per cent, we cannot but be impressed with the fact that the destruction of the cancer cell is as complete even in its early stages by radium as by any form of surgical extirpation. Radium has had its greatest triumph in the treatment of cancer of the cervix uteri.

The contention as to the relative value of operation or radium in Group I cases in some clinics is not definitely settled. In this country the radical operation is a matter of history. There is no difference in opinion as to the value of radium as a palliative measure in the treatment of all borderline and advanced cases, for with radium we can control the hemorrhage, heal the ulcer, and thus diminish the septic absorption and retard the extension. If we add to irradiation lymphatic block by the x-ray, or lymphatic block and circulatory starvation by abdominal incision, excision of the lymphatic chain and ligation of the internal iliac arteries, we can prolong the life of the cancer patient for a very considerable time and often cure the supposed incurable case.

Regarding malignancy of the body, it is an accepted fact that early total hysterectomy with bilateral salpingo-oophorectomy and wide excision of the round and infundibulopelvic ligaments, gives from 65 to 80 per cent of cures. This is accounted for by the fact that we have an early danger signal in body cancer; namely, a bloody uterine discharge which is always anomalous in a woman at or past the menopause. Every anomalous bleeding at this time should be regarded with suspicion and should be subjected to diagnostic curettage and examination of the biopsy specimen. Adoption of this plan will give a positive diagnosis of malignancy in nearly 50 per cent.

Now a few words of warning as to the dangers from diagnostic curettage. First, lymphatic avenues are opened and metastasis may occur. It is, therefore, well to precede the curettage with a hypodermic of pituitary extract, using one or two ampules to maintain the contraction of the uterus during the removal of the tissue for examination. Second, radium should be immediately introduced into the body in order that the lymphatics may be sealed. This furthermore presupposes that with the dilatation, curettage, and the introduction of radium, the vaginal flora have been transferred upward into the uterine cavity and explains the frequent temperature reactions which follow this simple diagnostic procedure. Experience has taught us that it takes from four to six weeks for the uterus to sensitize itself to this bacterial invasion and that if hysterectomy is done, say, a week after the introduction of radium, the operation will be followed by

death or by morbidity, while, if on the other hand, we wait for the uterus to sensitize itself, as Curtis has shown, and do not operate until from four to six weeks after the diagnostic curettage has been done and the radium inserted, the results will be satisfactory.

To summarize: We would say that in this country and Europe, radium has replaced the radical operation in the treatment of all cases of cervical cancer except possibly in incipient growths upon the portial surface. Even in these the high primary operative mortality more than balances the possible advantage of operation. In cancer of the body preoperative radiation followed by total hysterectomy with postoperative radiation is the accepted procedure. Our personal experience favors preoperative radiation a month or six weeks prior to extirpation.

20 LIVINGSTON STREET.

Neverman, H.: Foreign Protein Therapy in Inflammatory Tumors of the Adnexa.
Archiv für Gynäkologie, 1924, cxxii, 273.

Neverman used arthigon, turpentine, aolan, caseosan, and yatren injections in 208 cases of inflammatory tumors of the adnexa and checked them carefully by follow-up examinations averaging twenty-one months following the course of treatment. There were 411 cases in the Hamburg clinic during this same period which were not subjected to foreign protein therapy but were given only supportive treatment, symptomatic treatment, and absolute rest. There was practically no difference in the subjective or objective results in the two groups, and the author concludes that foreign protein therapy has no therapeutic value except for the psychic effect upon the patient. Those who receive this form of treatment feel better because they feel that something active is being done in their behalf, and this is of great value in private practice. He therefore believes that foreign protein therapy has a definite place in the treatment of inflammatory tumors of the adnexa.

RALPH A. REIS.

ABDOMINAL REPOSITION IN ACUTE INVERSION OF THE PUERPERAL UTERUS

By James Lincoln Huntington, M.D., Frederick C. Irving, M.D., and Foster S. Kellogg, M.D., Boston, Mass.

THIS paper deals with five cases of inversion of the uterus immediately after delivery. All were treated by abdominal operation with recovery in each instance. One of these patients has since been delivered normally twice without recurrence of the inversion. In another the condition was complicated by instrumental perforation of the uterus. Two cases were operated on two hours after delivery; one, four hours; one, ten hours; and one, thirty-six hours. All were transfused at the time of operation.

In three of these cases an attempt was first made at vaginal reposition, without success. In each instance hemorrhage was so profuse that the operator desisted and packed the vagina. In one of these cases, which had been delivered thirty-six hours, the cervix was found to be tightly contracted about the lower uterine segment. In the remaining two cases no attempt was made at manual restoration but laparotomy was resorted to forthwith.

After a completely inverted uterus has passed through the cervix that structure contracts around the lower uterine segment. Since the inverted fundus is much too large to be forced through the cervix the only way in which reposition can be effected manually is by inserting the tips of the fingers into the sulcus between the cervix and the lower uterine segment and making upward pressure. In this way that portion of the uterus which inverted last will undergo replacement first. It is this principle but carried out from above, that has been used in the abdominal operation performed upon these five patients. While we are aware that, favored by ample dilatation of the cervix, the recently inverted uterus has been replaced a number of times successfully, we nevertheless think that the abdominal method here described is attended with less risk and more certainty.

In the five cases reported in this paper we employed the operation devised by Huntington and described by him in the *Boston Medical and Surgical Journal* (April 14, 1921). The abdomen is opened by a low median incision. If there is complete inversion, the uterus is absent from the pelvis, there being a crater in the region of the cervix into which have been drawn the tubes, round ligaments and occasionally one or both ovaries. The operator and his assistant are both armed with two Allis forceps. Each inserts one of his forceps into the crater for

about an inch and grasps the surface of the uterus on his side. Both draw upward simultaneously, pulling a portion of the uterus out of the ring and restoring it to the peritoneal cavity. (Fig. 1.) Steadying the uterus by the forceps already applied the operators now insert their second forceps into the crater for about the same distance as before, again grasp the sides of the uterus and pull upward. Thus by successive bites and upward tractions (Fig. 2) the uterus is gradually restored to its normal position in the abdominal cavity. (Fig. 3.)

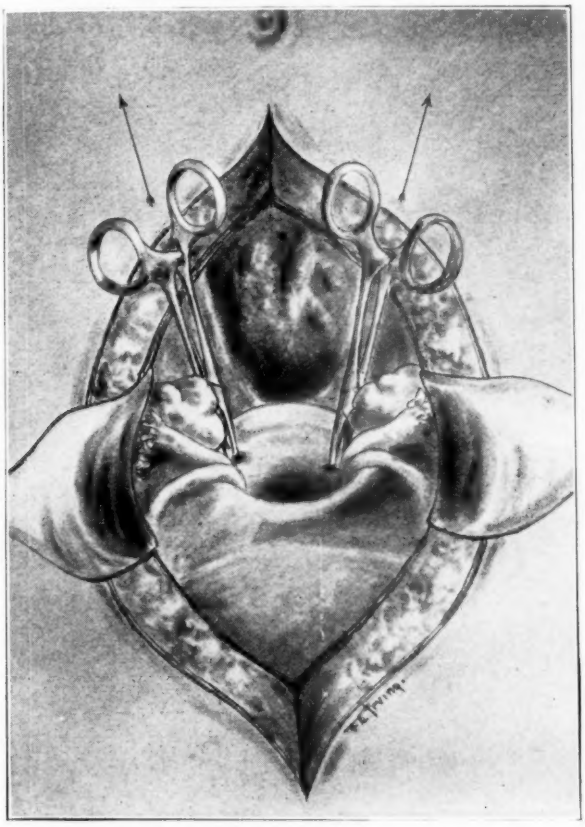

Fig. 1.

Since this paper is intended solely to demonstrate a method of treatment, we have attempted no collective review of inversion of the uterus as reported in the literature, nor have we thought it advisable to speculate upon the etiology of the condition.

CASE 1.—(Huntington) This patient, a 33-year-old para iii. had gone through a normal pregnancy, labor and puerperium with both preceding children. The present labor was terminated by easy low forceps at 6:20 A.M., Nov. 11, 1919.

Fifteen minutes later gentle pressure on the fundus revealed the placenta at the introitus and it was easily delivered. Moderate bleeding ensued and ergot and

pituitrin were given intramuscularly. The pulse was 80 but of only fair quality. What appeared to the assistant to be a rather nodulated fundus as felt through the abdominal wall seemed hard and well contracted. The bleeding continued and the pulse became a little poorer in quality although it still remained at 80. The patient's face grew pale and drawn and arrangements were made for a transfusion. Every five or ten minutes about half an ounce of dark blood would escape from the vagina. At the end of an hour transfusion was definitely decided upon and preparations were made to pack the uterus. Upon introducing the hand the

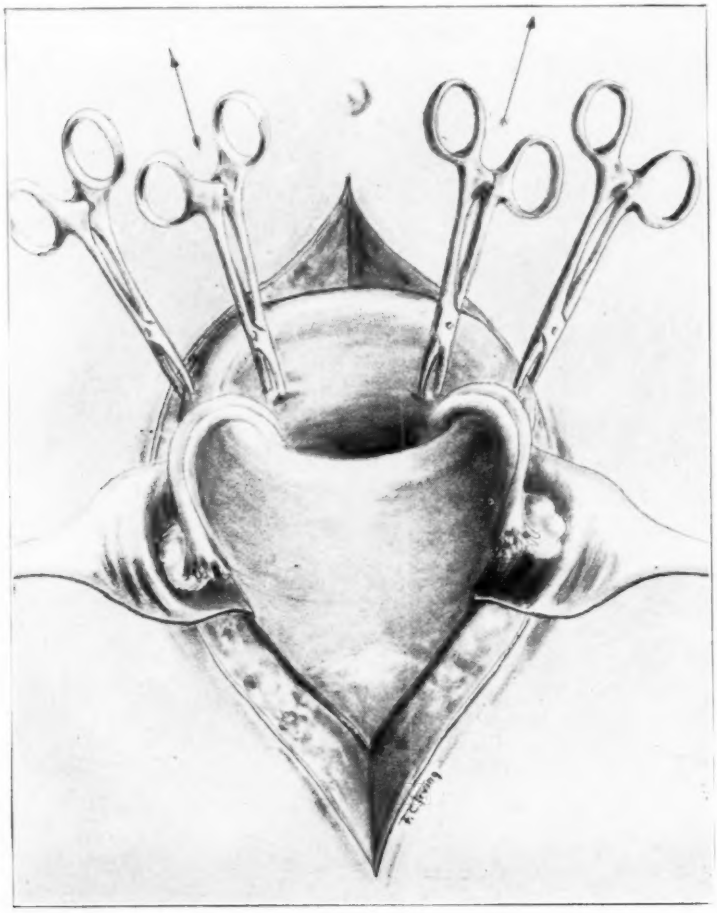

Fig. 2.

inverted fundus of the uterus was found projecting through the cervix, which was hugging it like a collar. When an attempt was made to effect reposition by pressure from below blood poured from the vagina. Immediate laparotomy was then done. The patient was almost pulseless. As the abdomen was opened a transfusion was started. Both appendages had been drawn into the crater. Reposition was effected by the method described above and the abdomen closed in layers.

By the time the transfusion was half over the patient's pulse was strong at the wrist and decreasing rapidly in rate. When the patient left the table her pulse was 90 and the systolic blood pressure 100.

The recovery was uninterrupted. Six weeks later pelvic examination revealed the uterus in anterior position, freely moveable, of normal size; the cervix long and conical. The os was practically intact and much smaller than is usually found in a multipara. There have been no further pregnancies.

Case 2.—(Irving) At 6:30 A.M., November 29, 1920, this patient was delivered after a seven hour primiparous labor by low forceps with the scalp in sight. The placenta, which was thought to have separated, was expressed by Credé's maneuver.

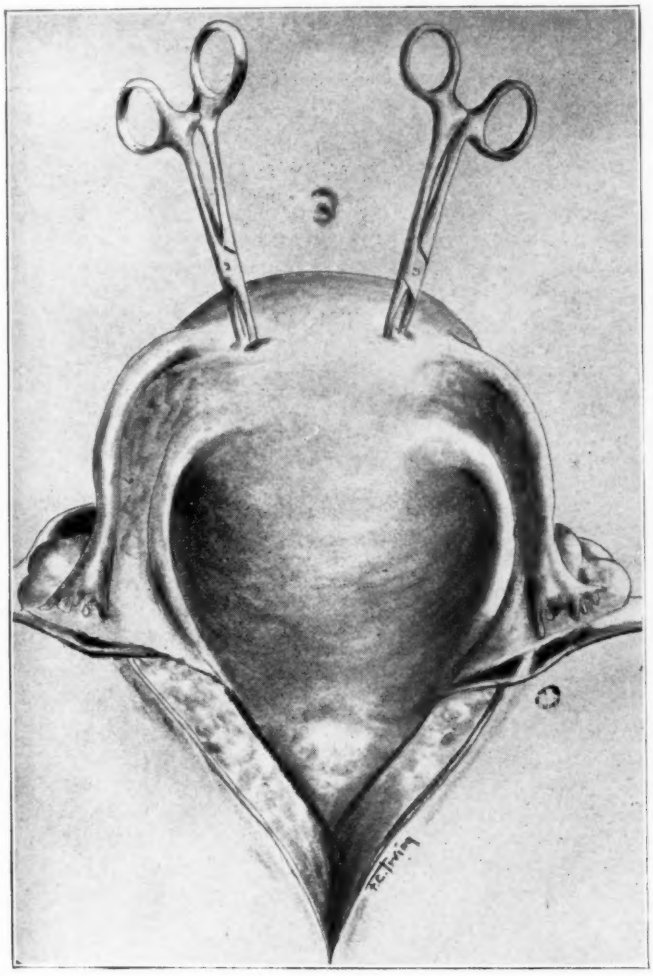

Fig. 3.

About one-half of the membranes were torn off and left in utero. The patient was then in good condition, her pulse being 112. Two hours later the pulse had risen to 132 and was of poor quality. There was more than the usual amount of bleeding. Thinking that the retained membranes were the cause of the hemorrhage the patient was etherized and the vagina was found to be occupied by a mass the size of a grapefruit. There was a small dimple on the left of the most dependent portion of this mass. Mistaking this for the cervix her attendant introduced a long Reynolds curette into it for the purpose of removing the membranes.

This instrument immediately disappeared up to the handle and was withdrawn. About this time an obstetrician was called in consultation. He examined the patient and stated that there might be an inversion of the uterus or that the uterus might possibly have been torn loose from its attachments.

The patient was first seen in consultation by one of us (F. C. I.) at 1:30 P.M. At this time a midline tumor reaching to within an inch of the umbilicus was found. There was no active bleeding but the patient was very pale; the pulse, perceptible at the wrist, was 140. When a five yard packing strip was removed from the vagina the mass which had been palpable in the lower abdomen disappeared and a completely inverted uterus was evident. The cervix was found to be fully dilated and in apposition with the walls of the bony pelvis. A small hole admitting a finger was discovered to the left of the fundus and somewhat posterior; undoubtedly where the curette went in. No attempt at replacement was made and the vagina was repacked.

At 4:00 P.M. the abdomen was opened, the patient being transfused at the same time with 700 c.c. of Group IV blood. The inversion funnel, in diameter about two inches, was found presenting. The uterus was replaced by the same method employed in Case 1. The perforation caused by the curette was closed with No. 2 chromic catgut interrupted and No. 1 chromic catgut continuous sutures. A cigarette wick was placed to the left of the uterus and the abdominal wound closed to the drain in layers. One ampule of pituitrin was given intramuscularly. The patient was in good condition on leaving the table. Her pulse was easily palpable at the wrist and of satisfactory quality. The vaginal pack was removed. There was no further bleeding.

The patient had an elevated temperature for several days and discharged some pus from the abdominal wound. Her convalescence was not unduly protracted and she was discharged from the hospital in good condition.

On July 7, 1924, the patient presented herself for examination. She had had no further pregnancies. There was at this time a slight bloody vaginal discharge, a small bilateral tear of the cervix. The uterus was of normal size and in anterior position. Nothing abnormal was made out.

CASE 3.—(Huntington) The first pregnancy of a 22-year-old para ii had been terminated by a breech delivery. The present pregnancy ended in the spontaneous delivery at 4:30 P.M., April 23, 1922, of a nine-pound, thirteen-ounce child which had presented by the vertex. There was no unusual amount of bleeding during the third stage of labor but as the placenta did not come away for thirty minutes it was expressed by Credé's maneuver, only a moderate amount of pressure being necessary. Since the bleeding which followed was somewhat excessive ergot and pituitrin were given intramuscularly. Five minutes later, as the loss of blood still continued the vagina was explored and the uterus found to be inverted. An attempt at replacement only resulted in an increase in the hemorrhage so it was abandoned and a vaginal pack introduced. The same abdominal operation was performed upon this patient and she was transfused simultaneously. Although she was almost pulseless when the abdomen was opened she rallied promptly and made an uninterrupted convalescence.

Since then this patient has had two normal deliveries without incident. On each occasion the placenta was removed manually from the vagina without resort to any pressure on the fundus.

CASE 4.—(Kellogg) This patient, a primipara, when seen in consultation by one of us (F. S. K.) at 4:00 P.M., July 29, 1924, had been delivered by easy low forceps early the morning before. There had been no traction on the cord and the birth of the placenta had been effected without effort by Credé's maneuver. The attendant had given what he considered to be an intrauterine douche for the hemorrhage which followed. A state of shock with a weak, rapid pulse supervened,

but the patient improved under treatment. Two hemorrhages occurred in the next thirty hours. The physician then found on examination a mass filling the vagina which he took to be an inverted uterus, a large myomatous polyp, or a combination of the two.

When seen in consultation the patient was pale, her pulse 120 and her temperature 99.° On abdominal palpation a tumor rising one inch above the symphysis was found in the midline but no central depression could be made out. On vaginal examination the uterus was found to be inverted and firmly gripped above by the tightly contracted cervix, which was dilated only about one and three-quarter inches.

At 7:00 P.M. an attempt was made to reduce the inversion *per vaginam*. Owing to the tightly contracted cervix this was found to be impossible and resulted in such profuse hemorrhage that it was immediately abandoned.

On opening the abdomen both tubes and ovaries were found drawn into the crater. Traction by Allis forceps easily restored the uterus to its position in the abdominal cavity.

The patient was transfused coincidently with the operation but was in a precarious condition for the first twenty-four hours following. Her convalescence was complicated by a moderate uterine sepsis and an attack of femoral phlebitis but she ultimately recovered.

CASE 5.—(Kellogg) The last patient was a 24-year-old para ii. Her family physician delivered her of her first infant by high forceps after a six and one-half hour labor on August 8, 1924. She made a normal convalescence.

Her present pregnancy was uneventful. She was delivered normally by an externe under supervision in the Boston Lying-in Hospital at 8:32 A.M., August 17, 1926, after four hours of labor. The placenta was expressed fifteen minutes later by Credé's maneuver with some difficulty. There was partial retention of the membranes. The pulse was 120, the color good. The uterus did not contract well and the fundus was found to present a dimple on palpation. The house officer was unable to introduce his hand into the uterus to discover if it was partially inverted as the cervix was tightly contracted. The patient then went into collapse with irregular respirations and a rapid pulse. She was pallid, the skin was cold, the lips slightly cyanotic and the eyes exhibited nystagmus. The patient became unconscious and the blood pressure fell to 50 systolic. More than the usual amount of blood postpartum escaped from the vagina. Under supportive treatment and while awaiting the arrival of a suitable donor for transfusion the pulse improved and the systolic blood pressure rose to 80.

At 12:20 P.M. the abdomen was opened and at the same time the patient was transfused with 500 c.c. of citrated blood. The uterus was found to be partially inverted, the fundus and both cornua being in the funnel with the distal ends of both tubes and the ovaries just outside the margin of the ring. Reposition was effected in the usual manner and was accompanied by a sudden and marked improvement in the patient's condition. The lips became pink, the pulse improved and the respirations became rhythmic. The wound was then closed in layers.

The patient made an uninterrupted recovery. On discharge the cervix was found intact and posterior, the uterus anterior and well involuted. The vaults were free and there was no uterine discharge.

SUMMARY

1. Five cases of acute puerperal inversion of the uterus are reported; four complete and one partial.

2. In three instances manual reposition was attempted without success and was abandoned and the vagina packed on account of hemorrhage.

3. Manual reposition in some cases is impossible and may be accompanied by such free bleeding that it is questionable if it should be attempted.

4. All five cases were easily and successfully treated by abdominal reposition of the uterus by the method here described.

5. All five cases were in such poor condition that they were transfused at the time of operation.

ENDOCRINE THERAPY*

By Robert T. Frank, A.M., M.D., F.A.C.S., New York City

ENDOCRINE therapy was based on a mistake. This most romantic chapter of modern medicine, which, paradoxically, links the science of today more and more closely with the humoral pathology of the ancients, began with the spectacular and fallacious report presented by Brown Séquard before the Société de Biologie of Paris, in 1888, dealing with the rejuvenating effect of testicular extract. Upon this insecure foundation, a tremendous superstructure has sprouted with mushroom speed. Again and again, because of the haste of its architects, the lack of solid foundation stones, and the weakness of its structural material, this airy scaffolding has threatened to topple and fall, but today, an ever increasing host of earnest and indefatigable workers are swarming busily, shoring, underpinning, aligning, reconstructing, and fortifying with solid facts, the sketchy skeleton which more and more is assuming the solid, safe, and balanced proportions of a completed edifice.

The first sound observations made in endocrinology were clinical. I instance Parry, who described exophthalmic goiter in 1825; Addison, who in 1855 gave a complete description of the pathology and symptomatology of tuberculosis of the adrenals, and Kocher and Reverdin, who in 1882 outlined the effects following removal of the thyroid gland (athyreosis).

As early as 1849 Berthold transplanted the testes of cocks and thus demonstrated the internal secretion of the testes. His important contribution aroused no interest. The first successful use of endocrine therapy was made in 1892 by Murray who gave fresh or glycerin extract of thyroid glands to a woman suffering from myxedema, and kept this patient in excellent health for a period of thirty-four years. This striking and wonderful result produced a frenzy of enthusiasm when it was fully appreciated. In consequence of this apparently simple method of gland therapy, it was hastily concluded by a large

*An address presented at the Joint Meeting of the New York and Philadelphia Obstetrical Societies, Philadelphia, April 12, 1927.

proportion of the profession that the problem of endocrine therapy had been solved. Every imaginable gland and body tissue was prescribed with most unanimous failure. It has taken years of study, of trial, and of exhortation, to bring the saner members of the profession to recognize that the problem is not simple. Only in the last few years has marked and encouraging progress been made.

In contradistinction to the ill-balanced haste with which endocrine therapy was taken up and exploited, the clinical study of endocrine diseases has progressed steadily and has now reached a considerable degree of perfection. The functions of the glands of internal secretion, with the exception of the thymus and pineal, as well as a large number of syndromes due to disturbance of their action, can be outlined with a considerable degree of assurance. The effect of the various glands upon metabolism and growth has been thoroughly studied, as well as their influence upon the nervous system, especially its autonomic division. Attempts to analyze the interrelation and interaction of the glands upon each other and the consequent development of polyglandular syndromes have not been as successful and still are in a hazy state.

Lately into the chaos of endocrine therapy, which has been a whirlpool of empiricism, charlatanism, and even gross fakery, a bright beam of light has penetrated. The voice of laboratory investigators who have been far removed from the clamor of the market place, the steadying suggestions of the pharmacologists, the revulsion of the disappointed enthusiasts, and the few voices raised from the onset in the cause of common sense and common decency, are beginning to be heard and hearkened to. In addition, the striking and incontrovertible effects of the few endocrine remedies which have been perfected tend to sober the clamorous crowd sufficiently to realize that potent endocrine substances in minute concentration produce sharply recognizable effects, and in overdose may cause severe symptoms of poisoning. Adrenalin, pituitrin, thyroxin, insulin, the parathyroid hormone, the female sex hormone, one and all, whether the partial hormone, i.e., druglike extracts like the two first mentioned, or the physiologically fully potent substitute, possess these qualities.

I therefore foresee in the immediate future, not only a return to sanity, but the demand for objective pharmacologic and physiologic criteria and proofs before the further employment of any endocrine remedies is resorted to.

After the introductory era of clinical investigation which first called to our attention the startling effects produced by the normal activity of the glands of internal secretion as well as the more dramatic and recognizable results consequent to disease of these glands, all substantial advances thereafter made have resulted from physiologic and

pharmacologic investigation. It is upon these that I desire to focus your attention.

Remember that the physiologist is in a predominantly favorable position to study the normal action of a given gland. He is able to practice complete or partial ablation as well as transplantation, and in certain instances can correlate the effect observed in experimental animals with the symptoms found in disease. With the help of the pharmacologist and chemist, he has attempted replacement and substitution therapy. This path has not been as easy as the first fortunate experience of Murray promised, because the thyroid gland appears to be the sole endocrine depot in which the active substance is found stored and ready for immediate use.

The pharmacologist and chemist first isolated a simple partial hormone, if I may coin this word, namely adrenalin. After its isolation, Aldrich and Takamine succeeded in synthesizing this substance (1901). Again our hopes were aroused to a high pitch, but today physiologists affirm that adrenalin exerts no influence on the bodily functions. Many barren years elapsed before Kendall isolated thyroxin and reported its formula, upon the accuracy of which, however, serious doubt recently has been cast by Harington who proposes an entirely different structure for this substitute for thyroid substance. Pituitrin, also a partial hormone, the product of the posterior lobe of the hypophysis, although readily extracted and apparently not very complex in its structure, has as yet resisted chemical isolation. Quite recently the powerful and toxic hormone, insulin, has been prepared by Banting, Best, and Collip, but it is not yet completely purified or isolated, and still more recently, Collip has presented us with a fairly active parathyroid hormone, as yet in somewhat crude form. Lastly, female sex hormone has been obtained in unstable but already usable concentration by several investigators, and an active anterior pituitary extract appears to be in its birth throes.

The real reason that such noticeable advance has been made in the last decade is solely due to the fact that the pharmacologist, physiologist, and chemist have finally supplanted the empiric investigator. *Each advance has been based upon the discovery or elaboration of some specific and pathognomonic test* for a given endocrine product. Without such specific test it is almost impossible to attempt either to find, purify, or isolate a hormone. Let me instance a few of these tests to convince you. Adrenalin in less than one-millionth dilution produces inhibition of the intestinal muscle, the uterine muscle of the pregnant cat responding with contraction; one milligram of thyroxin speeds up the basal metabolism 2 per cent; insulin reduces the blood sugar in definite proportion and in overdose causes hypoglycemia (one unit equals the amount required to induce convulsions in a 2 kilogram

rabbit); parathyroid hormone affects the calcium metabolism quantitatively and relieves the spasms of parathyreoprival tetany; the female sex hormone produces estrual phenomena in the castrate mouse or rat and initiates the sudden onset of puberty in the immature rodent. I do not hesitate to predict that as soon as a specific test is elaborated for the adrenal cortex as well as for the male sex hormone, active preparations will shortly be discovered.

We surely agree that all rational therapy must be based upon accurate diagnosis. Therefore, before either attempting to prescribe an endocrine product or to influence an endocrine gland by any therapeutic measure, the cause of the derangement, its gravity, and extent should be known. Otherwise treatment is purely experimental, empirical and with few exceptions, futile. To arrive at such a diagnosis, a thorough examination is essential.

The three most striking and frequent syndromes encountered have to do with the pituitary, the thyroid, and the ovaries, for in order to simplify my task and as is justified before two societies whose practice is limited to women, I shall confine myself to the discussion of female patients. Needless to say, if glycosuria, tetany, marked asthenia with pigmentation present themselves as leading symptoms, investigation of the pancreas, parathyroid, or adrenals cannot be omitted, but in the majority of cases, I repeat, the three glands that I have first enumerated will be the ones primarily requiring investigation.

The history plays an important rôle. From it the time of onset may be assigned to a given period of the life cycle: onset in childhood favoring an hereditary basis, in adolescence perhaps ascribable to remediable faults in hygiene, during maturity resulting from the stress of sex life or the undue demands necessitated by the struggle for subsistence, all of these differing from the involution of senescence. It is essential, too, to determine whether the disease is of functional origin, as so many of the nervous manifestations due to disturbance of the autonomic nervous system prove to be, some of them branching imperceptibly into the neuroses, others simulating or actually followed by hyperthyroid conditions; or organic, in which case definite evidence of organic changes can be elicited. Some symptoms are transitory, some progressive, some stationary. The progress to be expected is of importance from the viewpoint of prognosis as well as to evaluate the effect of therapy. Certain disturbances are self-limited, as the goiter of adolescence; some are stationary, as the eunuchoidism which manifests itself in high stature or infantilism which inhibits the development of the genital tract; some progressive, as the bone disturbances of acromegaly.

The physical examination should include not only the cardiovascu-

lar and renal systems as well as the routine employed by every careful practitioner, but also the recording of abnormalities of stature, preponderance of extremities over body length, gracility or thickness of bones, facies, posture, and quickness of response. The secondary sex characters are of importance; voice, amount of hair, hair distribution, texture of skin, the amount and distribution of the subcutaneous fat, and the psychic response should be investigated. Patients may be divided arbitrarily into two groups which may be designated as the plus or the minus. The plus class includes those who are quick, alert, with rapid pulse rate, fine tremor, increased reflexes, moist skin, and frequent flushes. The minus class are the reverse; their response is slow, their demeanor sluggish, their pulse slow and regular, the skin is dry, the hands steady, the reflexes are diminished.

Of importance are signs of exophthalmos including the usual lid symptoms. Prominence of the superciliary ridges, spacing of the teeth, and spade or taper fingers give a rough preliminary indication of the functional activity of the hypophysis. The size of the thyroid is deceptive, hyperactivity frequently accompanying a palpably small gland. Breast development, unless extremely atypical, is rarely of much value in diagnosis. Infantilism documents itself by gracility of the body, contracted bony pelvis, marked shortening of the vaginal fornices, as well as by hypoplasia of the cervix. The uterine fundus is such a variable quantity and responds so readily to ovarian activity that it cannot be taken as a guide unless hypoplasia is noted over a long period. The routine physical examination will rarely, except in advanced conditions, give more information than this. Additional information can be obtained only by means of more detailed and special examinations.

These should include at least the following special tests: basal metabolism, differential blood count (lymphocytosis of over 30 per cent is of significance), pituitary x-ray, visual fields, sugar tolerance (blood sugar and glycosuria), and tests for the contents of female sex hormone in the blood. By these examinations, however, we are able, in a great number of instances, to catalog a given patient and put her in the hyper- or hypofunctional group of disturbances arising from pituitary, thyroid, or ovary. In the rarer instances, on which I do not propose to focus your attention, the hypofunctions of the adrenal, pancreas and parathyroid may require investigation. I might add that hyperfunctional conditions of these glands are not recognized with the possible exception of hyperactivity of the adrenal cortex in childhood.

It naturally follows that in hyperfunctional conditions of the pituitary, thyroid, or ovary, our efforts should be directed toward toning down the hyperactivity of the affected gland. In the two first men-

tioned glands, complete ablation is contraindicated except in the presence of malignancy. In all three glands less radical toning down of the activity may be obtained by resection, and with the advance in the technic of x-ray therapy, we are able to control the amount of involution produced in the glands with a surprising degree of accuracy. It must not be forgotten that the activities of the glands may sometimes be favorably influenced by less direct measures. Iodine given in case of adolescent goiter usually proves curative, and in the exacerbation of exophthalmic goiter it apparently reduces the toxemia and lowers the basal metabolism, at least temporarily. Ovarian hyperactivity may in rare instances be influenced by reducing external erotic stimuli, by venesection as well as by general hygienic measures. I know of no means of influencing the pituitary gland indirectly, although such attempts have been made.

Hypofunctional conditions require stimulation of the respective glands and this is somewhat more difficult to effect. In the case of the ovary, small doses of x-ray, by killing off persistent atretic follicles frequently increase the ovarian function. This effect is not exerted on the pituitary or thyroid with an equal degree of certainty. In their case substitution therapy must be considered, to which I shall refer in more detail at once.

Naturally in the treatment of any of the symptoms, particularly of nervous ones which arise in the course of endocrine disturbances, purely symptomatic therapy must not be omitted. Loss of weight will require roborant treatment, rest, and increased diet. Obesity, whether accompanied or unaccompanied by thyroid underaction, demands exercise, carefully restricted diet, and usually an entire change of regimen. The assurances of the patient in regard to her physical activity and dietary abstinence are rarely reliable. Nervousness, whether due to thyroid poisoning or not, will require safeguarding from psychic traumas, together with rest and sedatives, among which luminal and bromides have proved the best. Tachycardia, when excessive, will necessitate the use of codeine. Atropine in sufficient dosage, is sovereign in the pains resulting from spastic contractions, especially those complained of in the abdomen and uterus. Adrenalin, pilocarpine, and pituitrin, have one and all proved of little help.

Turning now to direct endocrine organotherapy, our mainstay is thyroid substance. Its exhibition will produce an increase of the basal metabolism and it may therefore be employed to stimulate the life process of a given individual. Its most striking effects are naturally limited to those cases in which the thyroid is underfunctioning; that is, those which show a basal metabolism habitually more than 10 to 15 per cent below the normal. Unfortunately the majority of obese patients show a perfectly normal basal metabolism with, how-

ever, a depression of the ovarian function as our blood studies have shown. Our few attempts to stimulate the ovarian function by means of the female sex hormone are not sufficiently conclusive as yet to permit me to express a definite opinion. In these cases I consider it distinctly unwise to risk giving so-called stimulating doses of x-ray to the ovaries, as the margin of safety is too small. Except when thyroid overactivity is diagnosed a tentative use of small amounts of thyroid extracts is fully justified in order to determine the responses of the given individual to stimulation of the general body metabolism.

I do not propose to discuss the well-known and specific effects of insulin in diabetes although it has proved a boon to the surgeon, permitting operation with impunity even in the presence of severe glycosuria, nor those of the parathyroid hormone in tetany. These drugs appear to be complete or nearly complete substitution products just as the thyroid substance may fully compensate for the loss of the thyroid gland.

As is well known, pituitrin does not in any way replace the loss of the anterior portion of the pituitary gland. Its use in obstetrics, in intestinal paresis, and in diabetes insipidus is too well known to require comment. Attempts to produce an anterior lobe extract have been only partially successful. We know that such extracts in the laboratory can exaggerate the growth impulse of young animals and produce marked lutein overgrowth in the ovaries. Quite recently Zondek has announced that puberty can be ushered in by the implantation of adult (male or female) anterior lobe substance in the youthful mouse, an observation, which, if confirmed, proves that interrelation and interaction of glands can take place. However, no extract is at present available for therapeutic use.

In conclusion, I want to refer to the effect of active female sex hormone extracts in the human female, a chapter of therapy which is just beginning. Our position for accurately studying and evaluating the results obtainable with this extract is especially favorable because not only do we possess specific tests for identifying the female sex hormone as such, but also a diagnostic method which enables us to determine its degree of concentration in the circulating blood. Knowing also the source of the active substance, which is found in the follicle, corpus luteum, and placenta (the three forming the "gestational gland") the criteria demanded by the most exacting pharmacologist can be satisfied.

A number of investigators including Zondek, in Berlin, Pratt, in Detroit, my coworkers and myself in New York and Denver, have been tentatively trying out such preparations as we could produce or obtain. A few of the pharmaceutic houses are also preparing, for experimental use, weak but yet slightly potent preparations. I shall

confine my remarks to my own personal observations which are not numerous but extremely promising.

The extracts which we have used have been prepared in Denver by my coworkers, Dr. Gustavsons, H. Krueger, etc., and employed here in New York with the collaboration of Dr. M. A. Goldberger. The most potent extracts at our disposal have allowed us to inject from three to five rat units per day, which correspond roughly to from twenty-five to forty mouse units, which is the strength measure used by Zondek. Among the patients treated were some in whom menstruation never had occurred although they had reached adult age and their genitals were approximately normal to pelvic examination. A number of patients with persistent amenorrhea, in whom the absence of cyclical phenomena were assured by our blood test, were likewise injected. Two patients with conspicuous facial and body hirsutes are at present under treatment. I may say that all of these patients, after a week or ten days of daily injections, complain of tingling and fullness in the breasts and abdominal cramps. Upon withdrawal of the injections, these symptoms disappear without the appearance of the hoped-for menstrual bleeding. A number of patients volunteered the information that they feel stimulated in every way. This was most striking in a young girl with many stigmas of degeneration and infantilism, underweight and below par in every respect. However, such symptoms, although the patients are not enlightened as to what they may expect, and although everyone has described the same subjective phenomena, are not considered conclusive evidence by us, because we refuse to be influenced by criteria that are not strictly objective. In two patients with kraurosis of the vulva, one of whom had never menstruated and in whom vulvectomy was followed by a recurrence of the kraurotic atrophy and intense pruritus, immediate and as yet persisting relief of the itching was obtained. In both the mucous membrane and the vulvar outlet has assumed a different aspect, the dry, atrophic mucosa and skin showing normal vascularization and normal softness and moisture. In a third patient on whom a preparation obtained from an outside source was used, the treatment signally failed. One patient in whom a high blood pressure developed shortly after double oophorectomy, showed no reduction in the hypertension after two weeks of daily injection.

The female sex hormone as a therapeutic agent must therefore be considered as still in an entirely experimental stage. The outlook for it, however, would be extremely promising were it not for the great difficulty of obtaining concentrated solutions as well as of the great expense involved in purchasing the raw material, fresh ovaries now marketing at the price of over one dollar per pound.

In spite of many obstacles, endocrine therapy has at last emerged

from the unsatisfactory empiric stage. It has been placed upon a rational basis. Thyroid substance and thyroxin, insulin, parathyroid hormone, are well-established pharmacologic products. Adrenalin and pituitrin subserve limited, well-defined purposes. The female sex hormone is available in small amount for experimental and clinical investigation. Anterior lobe pituitary, adrenal cortex and testicular hormone are being studied. No decision as to the function, the potence or impotence of the thymus has yet been arrived at. And there we must leave the question for the present. The future promises great and rapid strides. Let us hope that this cheerful outlook will not again be dimmed by the uncritical acceptance of hearsay evidence by the enthusiast.

ADDENDUM

In reply to the various points brought out in the discussion, I would add that the so-called stimulating dose of x-ray is particularly to be avoided in cases of amenorrhea in which obesity coexists, as the margin of safety appears especially small in this type.

The question of giving desiccated whole ovary has repeatedly been raised. For the sake of argument let us say, and this is a most conservative estimate, that 100 grams of fresh sows' ovaries contain approximately 10 rat units if properly extracted and given hypodermically. This same amount of material given by mouth exerts only 1/20 of the parenteral effect. The simple mathematic result of multiplying 100 by 20 shows that 2 kilograms of fresh ovary would have to be swallowed by an unfortunate patient per day to exert a possible influence.

The question of sterility was raised in connection with the possibility that a key to the problem might be found in the basal metabolism. We have found as many sterile patients, and this includes only the group in which the husband is potent and the tubes found patent, who have a normal or an accelerated metabolism as those who have a minus basal metabolism.

I would like to emphasize that to obtain even the most exact data about a given patient is insufficient, because the interpretation and evaluation of the facts is so often difficult, misleading, or absolutely impossible. In regard to using the flushes of the menopause as a guiding symptom on the effect of therapy, I would simply say that close attention will show that as many patients who have not yet reached the menopause and whose sexual organs are functioning normally, suffer from flushes, as women who have artificial or physiologic menopause symptoms. These flushes may be classified as a symptom of autonomic imbalance.

Finally the case report of the gentleman who closed the discussion was highly illuminating just as he intended it to be. He told of a patient from whom both ovaries were removed, to whom he gave an extract of human corpus luteum, and the patient then became pregnant. Naturally his sole and kindly object in presenting this case was to reinforce my contention that the evaluation of seemingly incontrovertible data is so often misleading and impossible. Here an experienced and skilled operator felt sure that he had removed both ovaries but as is evident and as he emphasized some remnant was left behind which later regenerated and gave rise to the ovum which became impregnated.

10 EAST EIGHTY-FIFTH STREET.

A CASE OF RECURRENT TORSION OF THE FALLOPIAN TUBE WITH HEMATOSALPINX*

By John Casagrande, M.D., Brooklyn, N. Y.

THIS case is reported because it might be properly discussed as torsion of a normal fallopian tube of which there are only a few cases in the literature, the hematosalpinx apparently resulting from the torsion.

A thirty-six-year old multipara was admitted to the Brooklyn Hospital December 9, 1926, complaining of pain in the lower right abdomen. She had always been well except for an attack of influenza in 1918. Her menstruation was regular and painless, the last period on November 30, 1926. She had three uncomplicated spontaneous labors, the last, nine years ago; three abortions (two were induced), the last

Fig. 1.—Lumen of fallopian tube showing swollen plicae, with hemorrhage and edema; no organized tissue elements.

occurred in June, 1926, was spontaneous, and because of irregular bleeding which persisted, she was curetted at the Brooklyn Hospital, June 25, 1926. The discharge examination at this time revealed nothing abnormal in the pelvis. She had no febrile convalescences following any of her labors or abortions.

The first attack of the present illness began suddenly about the end of October, 1926 with a severe intermittent cramp-like pain in the lower right abdomen, which extended down the anterior side of the thigh and was accompanied by nausea and vomiting. At the end of thirty-six hours, the pain disappeared suddenly, and the following day her menstruation began. A vaginal examination then disclosed a cystic mass in the right fornix, measuring about 6 cm. in diameter; it was not tender. Abdominal palpation was negative.

*Read at a meeting of the Brooklyn Gynecological Society, March 4, 1927.

She remained entirely free from pain until the second attack, which occurred about six weeks later, December 8, 1926. The onset of this attack was similar to the first, but the pain was more severe and persistent. She entered the hospital the following day and remained under observation four days, during which time her pain gradually diminished.

Physical examination on entering the hospital disclosed that the patient was apparently suffering from pain; the right thigh was flexed on the body. There was rigidity of the lower right rectus and also tenderness in this region. A bimanual examination showed a parous introitus; the cervix had a bilateral laceration; the uterus was of normal size anteriorly but was pushed slightly to the left. The left tube and ovary were neither palpable nor tender. In the right fornix, there was a globular cystic mass of the size found previously, which was so exquisitely tender that no attempt to test its mobility was made. Her temperature varied from 100 to 101° F. The blood count on admission showed 12,600 leucocytes, a differential count of 88 per cent polymorphonuclear, 12 per cent small lymphocytes, hemoglobin

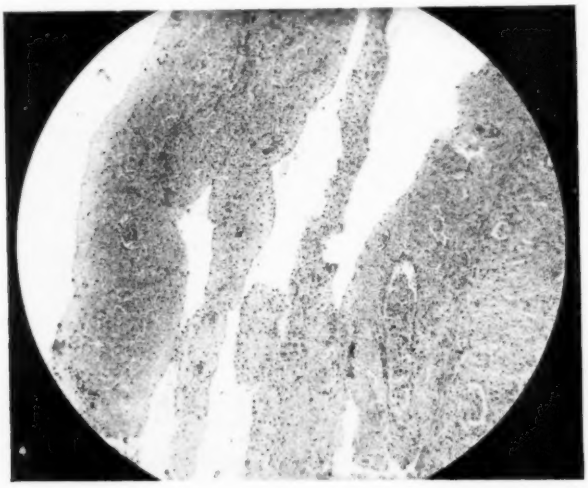

Fig. 2.—Another portion of tube, with some inflammatory infiltration.

82 per cent, and 4,640,000 red blood cells; coagulation time was 5½ minutes. Two days later, there were 14,500 leucocytes with 80 per cent polymorphonuclears and 20 per cent small lymphocytes. The urine was negative. The clinical impression during the first attack was ovarian cyst with a twisted pedicle; during the second attack a similar diagnosis was made plus a localized peritonitis.

On the fifth day after admission, a laporotomy was done. There was no blood or free fluid in the peritoneal cavity. The omentum was wrapped about the entire mass in the right side of the pelvis by fibrinous adhesions which were readily freed, exposing a bluish black globular right tube, the distal third of which was greatly distended, having a diameter of 8 cm., and filled with liquid blood. In the remaining portion of the tube, there were three complete twists. The right ovary contained numerous small cysts. The right broad ligament was abnormally long, having an elongated mesosalpinx. The right tube and ovary were removed. Appendectomy was done. Left tube and ovary were normal.

Her convalescence was uneventful, with primary union. She was discharged on the nineteenth day following operation, at which time the uterus was anterior; no tenderness or induration was present in either fornix.

A recent bimanual examination disclosed the same findings as on the hospital discharge examination. Her menstrual periods have been regular with a moderate dysmenorrhea.

The pathologic diagnosis was: necrosis and hemorrhage of the fallopian tube, follicular cysts of the ovary, and fibrinous periappendicitis.

The specimen consists of a cystic mass, measuring 8 cm. in diameter, which is covered with fibrinous and hemorrhagic adhesions. On the surface the tube can be made out; cross-sections, however, show no structure of tube. On opening the cystic mass, the cavity is filled with old and recent blood. The wall is necrotic. The portion of the tube not distended consists similarly of hemorrhagic black tissue without any structure. The ovary contains numerous small cysts, the largest measuring 2 cm. in diameter, having a hemorrhagic content and a smooth lining. The appendix is 5 cm. in length. The serosa is much congested. Cross-section shows a thick fibrinous and edematous wall. Microscopic sections of the cystic tube show no organized tissue that can be recognized; there is extensive polymorphonuclear infiltration. No decidual tissue was demonstrable. Section of the appendix shows fibrin and polymorphonuclear infiltration of the serosa.

COMMENT

Torsion of the normal fallopian tube is a comparatively rare condition. Darner has been able to find reports of only twelve authentic cases in the literature; however, in conjunction with ovarian cysts with twisted pedicles and pathologic changes in the tube, such as tubal pregnancy, hydrosalpinx, pyosalpinx or neoplasms, it is quite common. Anspach, who reviewed the literature in 1921, was able to find eighty-seven such cases. The mechanism of torsion of the normal fallopian tube may be explained by the theory of Payr, who experimently showed that venous congestion in a pedicle is conductive to torsion. This has also been described by Anspach. Payr injected the veins of the pedicle of a spleen that had been removed from the body and was able to produce a torsion of 125°, which he attributed to the fact that the veins of the pedicle are longer and more flexible than the arteries, and under the influence of passive congestion assume a spinal course and so tend to impart a twisting motion to the tumor. Smith and Butler, in a review of fourteen cases of apparently normal tubes which had undergone torsion, excluding those that occurred before puberty and during pregnancy, found that five out of the seven remaining cases occurred in close relation to the menstrual period.

In reviewing the literature, it appears that a large percentage of twisted tubes has an abnormally long mesosalpinx. In the case just reported, the two factors which appear necessary to bring on an attack were present; namely, a long mesosalpinx and circulatory disturbances caused by premenstrual hyperemia.

The subjective symptoms generally begin suddenly with severe pain in the right or left iliac fossa. Nausea and vomiting are very apt to follow the pain. Urinary disturbances, such as frequency, dysuria, and retention are common. If the tube readjusts itself these symptoms will completely subside; on the other hand, if the tube does not un-

twist the symptoms will continue. The objective signs will depend on the resulting pathology. If the process of torsion continues, there will be elevation of temperature, increase in pulse rate, leucocytosis, and a cystic mass will be palpated. The treatment is operation. If this is deferred too long, there may result a rupture of the tube or gangrene followed by peritonitis, or the tube may organize as a cystic or fibrous mass.

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30 Pierrepont Street.

A CASE OF SYMPUS DIPUS

By Morris Dreyfuss, M.D., New York City
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IT SEEMS from a fairly extensive survey of the literature that the occurrence of cases of sympus dipus is numerically somewhat uncertain, inasmuch as many authors assert their rarity, whereas more recently another mentions over seventy cases. Furthermore, there appears to be a dissension as to the exact classification of the cases, especially when more than one bone is missing from the thigh or leg. Many cases, thus, are classified as sympus dipus, when they really belong to the group of sympus monopus. According to Foerster, whose classification is most generally accepted nowadays, the monopus variety shows either a single, thick femur, occasionally with doubled epiphyses, or two femora, either closely pressed to each other or fused. There is only one bone present in the lower leg—sometimes a rudimentary second one; the foot is either defective or single or incompletely doubled. The dipus variety shows always two femora which are in closest contact, and two sets of bones in the lower leg; but sometimes only one fibula is present. In fact, the number of authentic and thoroughly studied cases of sympus dipus is rather small, and thus prompts the publication of this case.

The mother, twenty-three years old, Hebrew, has a negative family history; her husband's family history is also negative. At sixteen years she had scarlet fever, without complications. She has no previous obstetric record. Her last regular period was October 6, 1925. She had nausea and vomiting for the first two weeks, but afterwards her pregnancy had a normal course. Life was last felt on May 28, 1926 (eighth month). Labor pains started on June 6, 1926, when she was admitted to the Woman's Hospital. The foot presented; no life could be felt. The delivery was easy; the recovery of the mother uneventful.

The child was a monstrosity, known as sympus. The placenta was normal, also the amount of amniotic fluid. An autopsy was performed and these findings were recorded.

The newborn was apparently of the male sex. It measured from head to buttocks 27 cm., from buttocks to toes 20 cm. The umbilical cord contained one vein and only one artery. As far downward as the hip, no external anomalies were visible except that the right thumb was attached only by a thin bridge of skin, which made this finger more movable than the rest.

There was only one lower limb present, fixed at an angle of approximately 100°. The part of the limb which corresponds to the thigh measured 9.5 cm. in length,

Fig. 1.—Side view. Note the angle between the trunk and the lower limb, also the ridge carrying one of the fourth toes.

whereas the distance from the knee joint to the toes was 10.5 cm. Only one bone could be felt in the part corresponding to the thigh; in the lower portion of the limb three bones were palpable, apparently two tibiae lying laterally, and one fibula medially and posteriorly. In the region of the knee joint two lateral protrusions, suggesting two patellae, were visible. The circumference of the knee joint was 9 cm., of the ankle 5 cm. The knee joint was ankylosed, as well as the ankle joints. In the midline of the limb anteriorly a shallow groove was visible, extending downwards over the whole length. The patellae pointed backwards, while the popliteal space pointed towards the abdomen. The heels were also fused and faced anteriorly, as well as the soles of the feet. The two feet were united at the originally outer edges, forming a sharp ridge, which points backwards. The large toes were situated laterally. There were eight toes present; the first, second,

and third toes looked normal, whereas the fourth toes were placed one behind the other. The ridge carried one of those toes.

A distinct scoliosis to the left and a kyphosis were visible, both most marked in the upper thoracic region. A lordosis was present in the lower lumbar region. The anal opening was situated somewhat higher than normal and was not patent for a probe. Below this anal opening was a small raphe of 1 cm. length, with a small penis-like formation (0.8 cm.) at its end. Its free end was split into two small cone-shaped protrusions. Below this formation the scrotum, the size of a small pea, was visible, but it did not seem to contain the testicles. Two centimeters above the anal opening was a shallow groove in the skin, not covered with hair. The head was normal. The lungs appeared normal; they did not float on water. The thymus weighed 8 grams. The heart was broader than usual, the apex was bifid. The ventricles and auricles, and also the valves were normal. At a distance of 1.5 cm. from its origin from the ventricle, the aorta became very narrow. This portion measured 2 mm. in length and 4 mm. in diameter, when opened. After this constricted portion the vessel continued its course in the descending part of the aorta.

Upon opening the abdomen, a much dilated portion of the intestine hid the greater part of the abdominal organs, the situs of which otherwise was normal. The terminal portion of the intestine, comprising the sigmoid and the upper part of

Fig. 2.—Roentgenogram of the lower limb. It shows the fusion of the femora, the two Beclard's centers of ossification at their epiphyses, the two tibiae, and the single fibula.

the rectum, ended blindly in a conical stump. It was much enlarged, and was apparently filled with meconium. No kidneys were found, although the suprarenal bodies were in their normal positions. Attached to the under-surface of the left suprarenal was a small cystic body. Extending downwards from each suprarenal into the pelvic cavity was a duct of about 1 mm. diameter and approximately 4 to 5 cm. long; these ducts ended in a small oblong body situated near the occluded end of the intestine and at the bottom of the somewhat funnel-shaped pelvic cavity. This body is connected with the end of the intestine by loose connective tissue. On each side of the spine, on a level with the pelvic brim, and situated in the posterior part of the pelvic cavity, a normal testicle with attached epididymis was found. Their ductus deferentes likewise terminated in the above-mentioned oblong body in the pelvic cavity. The urachus extended from the umbilicus to this same body. No bladder or internal portion of urethra could be detected.

Roentgenograms of the body show the kyphoscoliosis of the thoracic and the lordosis of the lumbar portion of the spinal column. The vertebrae and the ribs showed no anomalies. Owing to the sharp angle and the ankylosis at the hip joint, it was difficult to get exact and instructive pictures of the pelvic bones, but the pubic bones were separated from each other in front by a wide space, and the sacrum was separated from the iliac bones. The femora were fused; their heads and trochanters were not visible, being probably cartilaginous. The upper portion of the fused shaft was somewhat broader than the middle portion; towards the lower one the shaft became very broad and chisel-like; there was a shallow groove

in the middle of the lower border of the femur. Slightly below this border and near the right and left outer edge a round, dense shadow indicated apparently the Béclard's center of ossification. The patellae were not visible. Two tibiae and one fibula were present. Directly under the lower end of the right tibia near the midline a large, round, dense shadow was visible and seven or eight metatarsal bones. The shadows of the phalanges were overlapping, and therefore, their exact number could not be ascertained. The metacarpus of the thumb could not be seen; there was one indistinct shadow in each phalanx.

Diagnosis: Monstrosity: Sympus dipus. Single umbilical artery. Hypoplasia of penis (diphallus partialis). Stenosis of isthmus aortae with patent ductus Botalli. Aplasia of right kidney, hypoplasia of left kidney. Atresia recti and ani. Aplasia of bladder. Bilateral retained testicles. Malformation of right thumb.

The interesting feature about this is not so much the fusion of the lower extremities, as the wide range of variety in the malformations of the internal organs. The changes in the urogenital system are similar to those of many other cases, also the malformation of the intestinal tract; both are almost constant features in sympus cases. What is different about our case and makes it somewhat rarer is the malformation of the heart and thumb, in addition to the other changes, as generally these changes occur only in the caudal portion of the body. The only almost constant feature in sympus is the single umbilical artery, and again single median umbilical arteries arising from the abdominal aorta so far have only been found in sympus. This is the pivotal point when we turn to the explanation of the causes of these malformations. Of all the theories which have been brought forward,—and they are far too numerous to be dealt with in this short report,—two are most outstanding, namely, Weigert's and Bolk's theories. Weigert (1886) asserts that this single umbilical artery arising directly from the aorta before its division is the persistent omphalomesenteric artery. As already mentioned, this single artery is present in almost all cases of sympus, and only in these monstrosities, and this could naturally lead to the conclusion that this arterial anomaly is the primary cause for the formation of the monstrosity. Weigert thinks that the other malformations are only secondary, due to malnutrition as a result of the impaired blood supply. The proof that the omphalomesenteric artery can persist together with both umbilical arteries has been furnished through at least one cause (Angenete). This theory of Weigert is opposed by many who take sides with Bolk. This author attributes the malformations to disturbances which affect the lower segments in earlier embryonic life and thus prevent the division of the lower extremities. His theory is very interesting, although in many points disputable, and he sees the causal origin in changes of the germ-plasm. This means that mechanical hindrances are considered by Bolk the main factors in the formation of these defects, whereas Weigert's theory is based upon an impaired blood supply and its sequelae. Which of the two theories is

the more plausible is difficult to decide, because both contain many well-founded points of explanation. In our case no facts for a sufficient explanation can be found, and it has simply to be added as another contribution to the list of cases of unsolved mysteries in congenital malformations.

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BIOCHEMICAL STUDIES OF HUMAN SEMEN AND ITS RELATION TO MUCUS OF THE CERVIX UTERI*

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I. INTRODUCTION

When the cervix of the uterus is examined by means of a speculum, a plug of mucus can be seen filling the external os. This plug is especially marked during pregnancy. The mucus fills the entire cervical canal and has the following characteristics: It is gelatinous in appearance, very viscous and adhesive in that it adheres tenaciously to either instrument or cotton applicator. When the mucus is pulled away from the cervix, it forms a slimy string which is broken with difficulty. In virgins and in those who do not present any pelvic pathology the mucus is semitransparent; but where there is a pelvic lesion such as an infection, a laceration, an eversion or erosion present, the cervical mucus becomes mucopurulent in character and probably more adhesive.

When one considers the passage of spermatozoa upwards by means of their own motility through the cervical canal filled with mucus, it becomes evident that there must exist some mechanism by means of which the character of the mucus is changed, so that it is no longer adhesive. For it is difficult to conceive of spermatozoa moving through such a gelatinous medium. The following experiments will show that there is present in the human semen a substance that changes cervical

*This paper is part of a thesis submitted by Dr. Raphael Kurzrok, in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

mucus from a viscous to a nonviscous compound and then dissolves it completely. The presence of this lytic substance may explain the mechanism by which spermatozoa are able to pass through the cervical canal into the cavum uteri.

The object of this work is to study certain phases of the chemistry of the semen and mucus, and to present data which may provide a deeper insight into the very important problem of human sterility by showing the existence of other possible etiologic factors of sterility.*

II. EXPERIMENTAL

A. *The Collection of Material.*—Semen was collected from healthy young males who were known not to have had either gonorrhea or syphilis. The semen was procured by means of the condom. Occasionally we were able to get friction specimens, the injection being made directly into a sterile container. Immediately after collection the semen was packed in ice and used for experimental purposes within twelve hours. Specimens older than twelve hours or not preserved properly in the cold were discarded. When one considers that the average ejaculation yields only from 3 to 4 c.c. of semen, one can understand why during a period of two years we were unable to secure more than 8 c.c. at any one time. Such a relatively large amount of semen we only possessed three times. About 500 properly collected semen specimens were obtained.

We had even less cervical mucus to experiment with. The normal cervix is 2.5 cm. long and its canal is spindle-shaped, being about 4 mm. in diameter at either os and 7 mm. at its center. The mucus was removed from the canal by means of a sterile uterine dressing forceps, after having cleaned the outer surfaces of the cervix with sterile cotton. Attempts at the removal of the mucus by suction led to the contamination of the mucus by blood; hence this method was not employed. The mucus was collected from women who had no pelvic lesion whatsoever. Since most patients in a gynecologic clinic have some form of pelvic pathology, only one patient in about thirty yielded a specimen which was suitable for experimental purposes. All specimens were immediately put into the ice box and used within six hours of collection. The average yield of mucus from a given patient was a fragment about 1.5 cm. long and 4 mm. in diameter, and weighing a fraction of a gram. On only a few occasions were we able to obtain several such specimens at one time. Another difficulty in the collection of the material was that on occasions when we had semen we were unable to get mucus, and vice versa. Furthermore, specimens from patients who had had natural intercourse within forty-eight hours were discarded for reasons which will be given below. In addi-

*We wish to thank Dr. I. C. Rubin who furnished us with a considerable amount of the material used during the first year of the work.

tion, no douching was allowed for two days before the collection of the specimen. About 300 proper specimens were obtained.

B. *The Action of Semen on Cervical Mucus.*—A freshly collected semen specimen containing about 3 c.c. was diluted with an equal amount of distilled water. A specimen of cervical mucus was divided into several fragments each measuring about 5 mm. by 3 mm. The mucus was then dropped into a test tube containing 2 c.c. of either 0.25 per cent sodium carbonate, or distilled water, or physiologic saline. To each tube was added 0.5 c.c. of semen diluted as above (or in some cases undiluted). Several drops of toluol or acetone were then added as a preservative. The tubes were stoppered with cotton and incubated at 37.5° for twenty-four hours. Table I shows the result of one such experiment.

TABLE I. SEMEN PLUS CERVICAL MUCUS

SUSPENSION FLUID	SEMEN	MUCUS	INCUBATION	DIGESTION RESULT
Distilled water	0.5 c.c.	shred	24 hr.	Complete digestion 3 plus
Distilled water	0	shred	24 hr.	No digestion 0
0.25 per cent sod. carbonate	0.5 c.c.	shred	24 hr.	Complete digestion 3 plus
0.25 per cent sod. carbonate	0	shred	24 hr.	No digestion 0
Physiol. Saline	0.5 c.c.	shred	24 hr.	Complete digestion 3 plus
Physiol. Saline	0	shred	24 hr.	No digestion 0

In all digestion experiments the following symbols will be used to denote the degree of digestion:
3 plus—Complete digestion. No mucus remains.
2 plus—Partial digestion. Slight fragment remains.
1 plus—slight digestion. Larger fragment remains.
0 —No digestion whatsoever. Entire fragment remains.

These tests showed that there was present in semen a substance which had a lytic effect upon a viscous cohesive mass of cervical mucus. The control fluids without semen had no action upon cervical mucus.

If the experiment was observed at regular intervals during the period of incubation, the following facts were noted: Within a half hour the mucus in those tubes containing semen had lost its glassy gelatinous appearance and had become dull. The edges of the shred became frayed and hazy in appearance. Finally after a period varying from twelve to twenty-four hours, depending on the activity of the semen, the mucous shred disappeared completely. In the control

tubes which did not contain semen the mucous shred remained the same size throughout and never lost its glassy and gelatinous appearance. The digested tubes, i.e., those which contained semen, showed a slight precipitate which upon microscopic examination was found to consist of dead spermatozoa, crystals, leucocytes, and epithelial cells, there being no sign of the mucus. Occasionally at the end of digestion there was seen floating in the solution a hazy faint cloud-like shred of mucus which upon gentle shaking disappeared completely.

C. *The Nature of the Lytic Substance in Semen.*—1. *The lytic substance was apparently specific for the mucin.* Using the technic as described, semen was allowed to act upon small shreds of egg white, casein, and fibrin. To each tube except the controls was added 0.5 c.c. of undiluted semen. Incubation was for twenty-four hours. Preservative was toluol.

TABLE II. SEMEN AND OTHER PROTEINS

SOLUTION	SEMEN	PROTEIN	DIGESTION RESULT
0.25% Sod. Carbonate	0.5 c.c.	cervical mucus	3 plus
0.25% Sod. Carbonate	0.5 c.c.	cervical mucus	3 plus
0.25% Sod. Carbonate	0.5 c.c.	fibrin	0
0.25% Sod. Carbonate	0.5 c.c.	fibrin	0
0.25% Sod. Carbonate	0.5 c.c.	egg white	0
0.25% Sod. Carbonate	0.5 c.c.	egg white	0
0.25% Sod. Carbonate	0.5 c.c.	casein	0
0.25% Sod. Carbonate	0.5 c.c.	casein	0
0.25% Sod. Carbonate	0	cervical mucus	0
Distilled Water	0	cervical mucus	0

The experiment (Table II) was repeated in media of varying P_H, both acid and alkali, with the same results. Semen did not digest casein, fibrin or egg white, under conditions at which it digested cervical mucus. The mucus is only with difficulty digestible by pepsin or trypsin.

2. *The lytic substance did not digest other types of mucin such as salivary or respiratory mucin.*

We were able to secure flakes of mucus prepared from the submaxillary gland.* The respiratory mucus was obtained by cough in a case of mild bronchitis. The sample was a sticky glairy shred somewhat

*The submaxillary mucin was kindly given to us by Dr. James Inouye of the Department of Biochemistry.

gray in color. The semen was used undiluted. Incubation was for twenty-four hours. Preservative was toluol. This experiment showed that under identical conditions semen did not digest mucin from the respiratory tract or the submaxillary gland, but did digest the cervical material.

TABLE III. THERMOLABILITY OF LYTIC SUBSTANCE

SOLUTION	SEMEN	MUCUS	DURATION OF BOILING	DIGESTION RESULT
Phys. sal.	0.5 c.c.	shred	10 min.	2 plus
Phys. sal.	0.5 c.c.	shred	20 min.	doubtful
Phys. sal.	0.5 c.c.	shred	30 min.	0
Phys. sal.	0.5 c.c.	shred	60 min.	0
Phys. sal.	0.5 c.c.	several shreds	0	3 plus
Phys. sal.	0	shred	0	0

3. *The lytic substance is thermolabile.*

The semen in this experiment was diluted with an equal volume of distilled water and boiled in a water-bath for various periods. It was then cooled and added to the cervical mucus and physiologic saline. Toluol was the preservative. The incubation period was twenty-four hours. Results of one typical experiment are shown in Table III.

This experiment showed that the lytic substance was thermolabile, and that boiling for thirty minutes on a water-bath was necessary before the substance was entirely destroyed. The tube containing the semen boiled only for twenty minutes showed doubtful digestion. The mucus had merely become less glassy and very slightly frayed at the edges, but did not diminish in size.

4. *The lytic substance did not deteriorate after five days in the cold.*

To a semen specimen several drops of toluol were added and the specimen placed in the ice box.

TABLE IV. LYTIC SUBSTANCE AND AGING

SOLUTION	SEMEN	MUCUS	DIGESTION RESULT
Phys. sal.	5 days old 0.5 c.c.	shred	3 plus
Phys. sal.	Fresh 0.5 c.c.	shred	3 plus
Phys. sal.	0	shred	0

This experiment demonstrated that semen which had aged for five days in an ice box and preserved by toluol, still maintained its ability to digest cervical mucus completely.

5. *The lytic substance was precipitated by phosphomolybdic acid.*

A specimen of semen was diluted with an equal amount of distilled water. To this phosphomolybdic acid was added drop by drop until no further precipitate appeared. The precipitate was voluminous, and the

supernatant fluid was clear with a faint yellowish tinge. The precipitate was filtered off and suspended in distilled water. The filtrate was used as such. Incubation was for twenty-four hours; toluol was used.

The results showed that the lytic substance was precipitated almost completely by phosphomolybdic acid, and that when the precipitate was resuspended in water it was still active. The action of the filtrate was doubtful. There was a slight fraying of the edges of the mucus but the fragment remained the same size. It is possible that not all of the lytic substance was precipitated by the single treatment with phosphomolybdic acid.

TABLE V. DIALYSIS OF SEMEN

SOLUTION	SEMEN	MUCUS	DIGESTION RESULT
Phys. sal.	0	shred	0
Phys. sal.	dialysate 2 c.c.	shred	0
Phys. sal.	dialysate 5 c.c.	shred	0
Phys. sal.	residue 2 c.c.	shred	3 plus
Phys. sal.	dial. 2 c.c. res. 2 c.c.	shred	3 plus

6. *The lytic substance did not dialize through a collodion membrane.*

Three collodion tubes of 20 c.c capacity were made. Five c.c. of semen were diluted with 25 c.c. of water and 10 c.c. of this mixture was placed in each of the collodion tubes. All three tubes were suspended in a beaker containing about 50 c.c. of distilled water. This was placed in an ice box for five days. Toluol was used as a preservative both inside and outside of the tubes.

The beaker and its contents were occasionally agitated. After five days the collodion tube showed a small amount of sediment at the bottom and a milky supernatant fluid. By shaking the sediment again became suspended in water. The water outside of the tube was clear and there was a slight sediment at the bottom of the beaker. This was also resuspended by shaking.

This experiment (Table V) showed that the substance in semen which exercised a lytic effect upon cervical mucus did not dialyze through a collodion membrane. The dialysate had no action upon cervical mucus.

7. *The Influence of the P_H on the lytic substance.*

A series of tubes containing 2 c.c. of phosphate buffer mixture was set up and to each was added a shred of mucus of approximately the same size. Both mucus and semen for this experiment came from the same patients. Owing to the insufficiency of material, the experiment was run in three stages of about one week apart.

These experiments (a typical result is given in Table VI) showed that at a P_H of 5.28 to 5.90 the lytic substance in semen showed its greatest activity on the acid side of neutrality. From a P_H of 5.90 to just beyond neutrality there was little digestive action. At a P_H of 7.37 and 8.04 there was the same optimum lytic activity. Other experiments showed that beyond a P_H of about 10 both semen and control tubes showed equal digestion, thus showing that the concentration of alkali in both was the causative factor in the digestion. There was no digestion at a P_H below 4.0.

TABLE VI. THE LYTIC SUBSTANCE AND THE P_H OF THE MEDIUM

P_H	SEMEN	MUCUS	DIGESTION RESULT
5.28	0.75 c.c.	shred	3 plus
5.28	0	shred	0
5.90	0.75 c.c.	shred	3 plus
5.90	0	shred	0
6.64	0.75 c.c.	shred	1 plus
6.64	0	shred	0
6.97	0.75 c.c.	shred	1 plus
6.97	0	shred	0
7.37	0.75 c.c.	shred	3 plus
7.37	0	shred	0
8.04	0.75 c.c.	shred	3 plus
8.04	0	shred	0

8. *The relation of the lytic subtance to the presence of spermatozoa in semen and its action in a case of Froehlich's Syndrome.*

Semen specimens were obtained from various patients who presented the following characteristics.

Semen *K* was from a normal fertile individual whose semen was known to digest cervical mucus actively. It contained a normal number of motile spermatozoa.

Semen *R* was obtained from a case presenting a distinct Froehlich's Syndrome. The wife of this patient was normal. Their marriage was sterile. The semen showed a few dead spermatozoa.

Semen *A* was from a patient who had a previous bilateral operation for hydrocele. The semen contained no spermatozoa. His wife was normal. Their marriage was sterile.

Semen *B* was obtained from a patient who had an attack of mumps during childhood. Both testicles were normal. The semen contained a normal number of actively motile spermatozoa. His wife was normal. Their marriage was sterile.

Semen *Ar* was obtained from a normal male. Numerous motile spermatozoa. His wife had an uncorrected adherent retroversion and their sterility was accounted for by the pelvic lesion in the wife.

All the cervical mucus used in this experiment was from a single patient; hence the experiment was carried on for over a period of a number of weeks.

These experiments (Table VII) demonstrated the following: The activity of the lytic substance did not depend on the presence of spermatozoa. Case A had no spermatozoa yet the lytic activity of the semen was normal. Case B had a normal number of motile spermatozoa, yet the lytic activity was only slight. In a case of Froelich's Syndrome the spermatozoa were few and dead and the lytic activity was very slight.

TABLE VII. THE LYTIC SUBSTANCE AND THE PRESENCE OF SPERMATOZOA

SOLUTION	SEMEN	MUCUS	SPERMATOZOA	DIGESTION RESULT
Sod. carb.	K	shred	normal, living	3 plus
Dis. water	K	shred	normal, living	3 plus
Sod. carb.	R.	shred	very few, dead	1 plus
Dis. water	R	shred	very few, dead	1 plus
Sod. carb.	A.	shred	none	3 plus
Dis. water	A	shred	none	3 plus
Sod. carb	B	shred	normal, living	1 plus
Dis. water	B	shred	normal, living	1 plus
Sod. carb.	Ar.	shred	normal living	3 plus
Dis. water	Ar.	shred	normal living	3 plus
Sod. carb.	none	shred	------	0
Dis. water	none	shred	------	0

9. *The lytic action occurred both in vivo and vitro.*

A specimen of mucus was obtained from a patient eight hours after natural coitus. There was no douching following this intercourse. Mucus from this patient had been used on other occasions for some experiments, and was completely digested by the semen of her husband. All previous experiments were in test tubes and properly controlled.

TABLE VIII. ACTION OF SEMEN IN VIVO AND VITRO

P_H	DIGESTION RESULT
5.58	3 plus
6.97	3 plus
8.04	3 plus

The cervix on this occasion was very clean. The mucus was only present in the cervical canal, was very small in amount, thin, lusterless, and had no adhesive properties. A shred of the mucus was added to 2 c.c. of phosphate mixture. No semen was added. Toluol was the preservative. Incubation was for twenty-four hours.

This experiment (Table VIII) showed that digestion had been going on in the cervical canal and that the partially digested mucus continued to complete digestion in vitro at a P_H ranging from 5.58 to 8.04.

10. *The lytic substance was not found in a bull's testicle.*

A fresh bull's testicle was stripped of its capsule and ground in a meat chopper. To 25 gm. of ground testicle 25 c.c. of distilled water was added and the mixture ground thoroughly with sand. Toluol was added and the extract was allowed to stand in the ice box overnight. It was then strained through cheese cloth and filtered by suction and then used.

The extract was added to the mucus, which had already undergone partial digestion in the cervix as described in the previous experiment and to normal mucus from another patient.

This experiment (Table IX) showed that our extract of bull's testicle did not digest human cervical mucus, and that it stopped digestion in mucous specimens that had already undergone partial digestion in the cervix, and which had undergone complete digestion in test tubes at different hydrogen-ion concentrations without any further addition of semen.

TABLE IX. THE LYTIC SUBSTANCE IS ABSENT IN A BULL'S TESTICLE

P_H	MUCUS	BULL'S EXTRACT	DIGESTION RESULT
5.58	Partially digested	1.0 c.c.	0
5.58	Partially digested	0	3 plus
6.97	Partially digested	1.0 c.c.	0
6.97	Partially digested	0	3 plus
8.04	Partially digested	1.0 c.c.	0
8.04	Partially digested	0	3 plus
——	Normal not digested mucus	1.0 c.c.	0
——	Normal not digested mucus	2.0 c.c.	0

11. *The activity of the lytic substance is diminished by the presence of pus in the cervical mucus.*

Three types of mucous specimens were used in this experiment. One was from a normal patient. The second specimen was from a patient with a leucorrheal discharge due to a lacerated cervix. The mucus had a grayish appearance, was opaque and glistening. The third specimen was from an acute gonorrhea. The mucus was thick, opaque, and was clinically frank pus.

TABLE X. LYTIC ACTIVITY AND CONTAMINATION OF MUCUS

SOLUTION 2 c.c.	SEMEN	MUCUS	DIGESTION AFTER 24 HOURS	DIGESTION AFTER 48 HOURS
Phys. Sal.	0.5 c.c.	Normal	3 plus	
Phys. Sal.	0	Normal	0	
Phys. Sal.	0.5 c.c.	Leuchorrheal	Doubtful	2 plus
Phys. Sal.	0	Leuchorrheal	0	0
Phys. Sal.	0.5 c.c.	Gonorrheal	0	Doubtful
Phys. Sal.	0	Gonorrheal	0	0

This experiment (Table X) demonstrated that as the amount of pus in the mucus increased, the mucus became more resistant to digestion. When frank pus was present there was almost no digestion in forty-eight hours.

12. *The nature of the end-products after the action of semen on cervical mucus.*

An attempt was made to determine how far the mucus was split by the lytic substance in the semen. That some change occurred in the mucus after digestion could be seen from the fact that the digested mucus gave no precipitate with acetic acid. It was thought possible that the prosthetic group—mucoitin sulphuric acid—was split off from the protein fraction of the mucus. In the absence of any reaction that could be used to determine the presence of a very minute quantity of this group, we were unable to test for it. It was impossible to isolate the prosthetic group by the method of Levene in view of the minute quantities of material with which we had to deal.

Thinking that perhaps the mucoitin sulphuric acid was split up, we tested for glycuronic acid by the Tollens napthoresorcinol reaction. The tests were always negative. We also attempted to test for hexosamine acetic acid by the Ehrlich reaction. The results were inconclusive. Occasionally we felt that we got a positive test for the substance after the mucus had been digested, but a repetition of the experiment under identical conditions, with the semen and mucus from the same patient, failed to give a positive reaction. Since almost nothing is known concerning the protein fraction of mucus, we were unable to approach the problem from that angle in view of our lack of material.

D. *The Reducing Action of Semen on Thionin.*—In efforts to make more evident, visually, the fragmentation of the mucous shred under the influence of semen, we stained the shred, before digestion, with thionin; when this stained shred was subjected to semen action, we noted that the thionin was reduced to a colorless compound. A preliminary study of this reducing power in semen is reported below and will be further continued.

A 0.001 per cent aqueous thionin solution was used. Incubation was at 37.5° C. for twenty-four hours. Toluol was the preservative. Semen was added as noted in Table XI, which gives the results of a typical test. 0.3 c.c. of the thionin solution made up to 2 c.c. with distilled water was used each time.

The thionin was decolorized by the semen.

1. *The decolorizing substance is thermostabile.*

A specimen of semen was boiled for three hours. Before the boiling, and at intervals during it, 0.5 c.c. samples of the semen were removed, added to a thionin solution and incubated for twenty-four hours.

TABLE XI. ACTION OF SEMEN ON THIONIN SOLUTION

THIONIN	SEMEN	RESULT
2.0 c.c.	1.0 c.c.	Colorless
2.0 c.c.	0.5 c.c.	Colorless
2.0 c.c.	0.25 c.c.	Colorless
2.0 c.c.	0	Purple

The experiment (a typical result is given in Table XII) showed that boiling semen for three hours did not destroy its ability to decolorize thionin.

TABLE XII. THERMOSTABILITY OF DECOLORIZING PRINCIPLE

THIONIN	SEMEN 0.5 C.C.	RESULT
2.0 c.c.	Fresh	Colorless
2.0 c.c.	Boiled ½ hour	Colorless
2.0 c.c.	Boiled 1 hour	Colorless
2.0 c.c.	Boiled 2 hours	Colorless
2.0 c.c.	Boiled 3 hours	Colorless
2.0 c.c.	0	Purple

2. *The decolorizing principle is precipitated from semen by phosphomolybdic acid, by saturation with ammonium sulphate, and by 95 per cent alcohol. It is not present in the filtrates from these precipitates.*

To a specimen of semen phosphomolybdic acid was added until no further precipitate resulted. The precipitate was filtered off and suspended in distilled water.

To 3 c.c. of semen an equal volume of 95 per cent alcohol was added. A white precipitate resulted which was filtered off and then suspended in saline. To another specimen an equal amount of distilled water was added and then ammonium sulphate to saturation. A heavy precipitate resulted. The precipitate was suspended in distilled water.

The experiments demonstrated that the decolorizing principle in a semen was precipitated by phosphomolybdic acid, 95 per cent alcohol, and by complete saturation with ammonium sulphate. The filtrates of these precipitates did not contain this principle.

3. *The decolorizing agent passes through a collodion membrane.*

Three c.c. of semen were diluted with 7 c.c. of distilled water and placed into a collodion tube. This was suspended in a beaker containing 25 c.c. of water and allowed to dialyze for five days in an ice box. Both dialysate and residue when added to a thionin solution either separately or together decolorize it.

E. *Other Properties of Semen.*—Human semen, boiled or unboiled, did not cause the production of a blue color with guaiac or benzidin, with or without hydrogen peroxide. This suggests the absence of a peroxidase or oxidase system.

Tests for glutathione* were uniformly negative in the semen.

Ether-alcohol extraction of semen yielded small amounts of a yellow oily substance. Identification and thorough study has thus far been impossible, because of lack of sufficient amount, but the substance contained lipin material, and in its reaction with bromine or iodine indicated a considerable degree of unsaturation. This unsaturation is perhaps of interest in relation to the hydrogen transport mechanisms involved in the reducing power of the semen.

Semen was found to contain catalase as evidenced by the rapid decomposition of hydrogen peroxide.

III. DISCUSSION

Sterility is assuming increasing importance, for it has been shown that sterility is on the increase. The problem presents many complexities, and especially complex is the case of the sterile woman whose past history is negative, whose physical condition is good, who presents no endocrine disturbance, has no pelvic pathology, has patent fallopian tubes, and whose husband shows normal motile spermatozoa. When such a patient remains sterile in spite of the usual forms of treatment, one must admit that there are other conditions which must be present before that patient can become pregnant. In other words, there are etiologic factors of sterility which have not been described. The absence or diminution of the lytic substance in semen may be such an etiologic factor.

When spermatozoa are deposited in the posterior culdesac of the vagina, it is essential that they reach the ovum within forty-eight hours after ejaculation. Mall[5] in an excellent paper published after his death, referring to human conception, concluded that it is probable that spermatozoa had lost their fertilizing power by the time they had passed the tube, and that any other conclusion entails many contradictions and unnecessary assumptions. Graf Spee[2] states that the duration of life of spermatozoa in the genital tract of a woman does not exceed twenty-four to thirty-six hours. Bryce and Teacher,[1] and Triepel[11] also concluded that fertilization must occur within forty-eight hours after copulation. Lillie[3] states, "The mere fact that spermatozoa may retain their motility in the human genital tract for three weeks or more (Waldeyer[12]) by no means proves that they re-

*Other experiments showed that glutathione was present in the testicle of full grown bull. It was present in an early corpus luteum and absent in the remaining portion of the ovary. Glutathione was not found in follicular fluid nor in the ovarian tissue that remained after the fluid was aspirated. A corpus luteum beginning to undergo degeneration did not give the nitroprusside test.

Furthermore in preliminary experimenting with follicular fluid it was found that it dissolved cervical mucus, reduced thionin, and showed the presence of a peroxidase. Semen inhibited the action of the peroxidase. A mixture of semen and follicular fluid did not decolorize thionin. Follicular fluid appeared to have an activating influence upon spermatozoa, and possibly a chemotactic influence.

Semen appears to be very strongly buffered, a fact of considerable clinical significance.

These subjects are still under investigation and will be reported upon subsequently.

tain their fertilizing power all this time, although this has been almost universally believed." Lillie demonstrated conclusively that spermatozoa of marine forms may remain motile for a long time after they have lost their power of fertilization due to the loss of their fertilizing agglutinable substance. Motility, then, is not a criterion of fertility.

When there is complete loss of the lytic substance, spermatozoa cannot pass through the cervical canal into the cavum uteri and then into the fallopian tube. Fertilization does not occur and the patient remains sterile. In the case where the lytic substance is diminished many hours may be lost by the spermatozoa before they can penetrate the column of mucus. By the time they have reached the tube they may have lost their fertilizing power although their motility may remain.

The same explanation holds true when the cervical mucus is contaminated by abnormal discharges. A woman with an acute gonorrhea with its extensive purulent cervical discharge, or with extensive leucorrhea due to tears or disease in the cervix almost never becomes pregnant as long as the discharge lasts. We have demonstrated that the lytic substance will not digest a purulent cervical mucus; hence spermatozoa will not pass through, and the patient will remain sterile. Where the cervical mucus is only partially contaminated, a considerable time may elapse before digestion is sufficient to allow spermatozoa to pass through the cervix. So that here, as above, by the time the spermatozoa have reached the tube their fertilizing power may be lost although their motility may remain. The patient remains sterile.

Rubin[9] has observed clinically that after natural coitus a contaminated cervix looks much cleaner, the mucus having been dissolved. Here, then, we observe clinically the presence of the lytic substance in semen.

The specificity of the lytic substance is a very interesting phenomenon. Not only are proteins such as fibrin, casein, or egg white not digested, but the closely resembling submaxillary and respiratory mucins are also not digested. Just how far cervical mucus varies from the other types of mucus we are unable to state. We have been unable to secure sufficient mucin from nongravid patients in order to make the necessary tests. An attempt will be made to secure mucus from patients in labor, but whether such mucus is the same as the mucus from a nonpregnant cervix, we are not in position to state. On theoretic grounds there is a possibility that cervical mucus varies with the function of the ovary, that is, mucus of the nonparous cervix differs from that of the pregnant cervix and from that in a case of amenorrhea due to endocrine dysfunction.

The fact that the lytic substance is precipitated by phosphomolybdic acid and does not pass through a collodion membrane suggests that it

is associated with the protein fraction of semen. These factors plus its thermolability, its optimal activity at a definite P_H, and its specificity, point strongly to the supposition that the lytic substance is an enzyme. Considering the complexity and specificity of spermatic fluid, it is not at all surprising to find such a highly specific enzyme in it.

An interesting speculation in this connection is the possible manner in which the sperm penetrates the zona pellucida, a rather thick, highly refractive, clear, glistening membrane immediately surrounding the ovum. Physically, therefore, it resembles mucin. Chemically, according to Minot[7] it (the zona pellucida) is resistant to acids, and soluble in alkalies only with difficulty. This makes its resemblance to mucin still greater. The sperm must penetrate this membrane in order to reach the ovum. Having expended considerable energy to reach the ovum in the tube, it is doubtful whether it could pass through this tough membrane by mere mechanical motion. Granting that the zona pellucida is composed of mucin, a minute trace of this lytic enzyme carried along by the sperm would explain the passage of the sperm through the membrane with an expenditure of but very little energy.

The study of the effect of the P_H on the lytic substance in semen showed that there are two zones of optimal activity on the hydrogen ion scale. One zone lies on the acid side, at a P_H between 5.28 and 5.90, and the other at a P_H between 7.37 and 8.04. There is some activity in the zone between these two peaks. This enzyme varies from the others in that the latter present only one peak on the hydrogen ion scale. But the conditions present in the human genital tract show why two such peaks are necessary. The cervix is constantly discharging mucus into an acid vagina. The vaginal P_H of the average healthy adult woman is 4.7 (Zwolinski and Truzkowski[15]). The normal cervix dips into the posterior culdesac which, with the woman in the prone position, forms a distinct depression known as the "receptaculum seminis." The injected semen accumulates in this depression, and the external os of the cervix dips into the "Samensee," as it is called by the Germans (Nuernberger[8]). The semen here must act on the cervical mucus which has been in an acid medium, hence the necessity for an enzyme that is able to digest mucus in an acid medium. When the spermatozoa pass into the cervix, they are in an alkaline medium, for the reaction of the cervix is just alkaline to litmus (Zuntz[14]). There is here the necessity for an enzyme that is able to digest mucus in an alkaline medium. The lytic substance in semen, by having an optimal activity on both the acid and basic sides of neutrality, fulfills both of the conditions.*

*It is possible that we may be dealing with two enzymes, one acting in an acid and the other in an alkaline medium.

The relation of the lytic substance to the presence of spermatozoa is an important clinical consideration. Taking the case of the patient B. for an illustration: This couple had been married for a number of years, and Mrs. B. never became pregnant. She presented no pelvic lesion, her history was negative, her general health excellent. The semen of the husband showed the presence of a normal number of actively motile spermatozoa. This would have been considered a normal semen specimen, but we have been able to show that this specimen could barely digest cervical mucus. This finding suggests a possible cause for the sterility in this case.

Patient R. presented clinically a Froehlich syndrome. Only a few dead spermatozoa were found in his semen. At the same time his semen digested mucus only slightly. Usually cases of Froelich syndrome are sterile. Whether both deficiencies are present in the semen of cases of Froelich syndrome or only one deficiency, we are unable to state, because this was the only case of this type that we had occasion to observe.

Are all the normal mucous specimens digestible by semen having the lytic enzyme? Up to the present time all normal cervical mucus was found digestible. It is possible that, when more mucus specimens are studied, some may be found to be undigestible by any semen specimen. In the cases where we have been able to match the husband's semen against his own wife's mucus, in fertile couples, digestion always occurs. Again, it is possible that in a very large series of cases, specimens of semen may be found that may be unable to digest the mucus of their wives but may be able to digest the mucus of other women. Such circumstances would explain the cases where a given couple is sterile and upon separation and remarriage to others each party has children. Only a prolonged study of the lytic phenomenon will shed further light on these interesting possibilities.

The fact that we were unable to demonstrate the lytic substance in a bull's testicle does not prove that it is absent there. It is very possible that our methods of extraction were insufficient. It is possible that its origin is elsewhere as in the prostate or seminal vesicles. The isolation of the lytic substance may prove to be of therapeutic value in cases lacking this enzyme. The observation that the addition of testicular extract to digesting mucus stopped further digestion need not be explained on the basis of a species specific inhibitory action. Other factors could have inactivated the lytic enzyme already present in the digesting mucus.

The decolorization of thionin presents probably a hydrogen transport system. The system is thermostabile. Thionin forms the hydrogen acceptor and upon taking up hydrogen forms the leuco base. The properties of the hydrogen donator are its precipitability by ammonium sulphate, 95 per cent alcohol and phosphomolybdic acid. It

is dializable through a collodion membrane. The hydrogen carrier is not glutathione because we have never been able to demonstrate its presence in semen. There is a possibility that it is an unsaturated compound such as we found by the alcohol-ether extraction. It may be of the type of linolenic or arachidonic acid, for each of these compounds has several double linkages.

The function of this activated hydrogen system in semen may be as follows: The lytic substance in semen may, by cytolosis of the zona pellucida, initiate the tremendous oxygen consumption by the ovum (Warburg,[13] Shearer[10]). The membrane may thus become permeable so that, according to Loeb,[4] "certain substances which were previously solid are liquified and allowed to diffuse into the egg, where they start or accelerate the chemical processes underlying development." (Quoted by Marshall.[6]) It has been shown in marine forms that if this cytolysis or oxidation be allowed to go unchecked, the eggs, although they begin to divide, eventually undergo complete cytolysis and die. A second corrective process is necessary to save the life of the cell. Experimentally this corrective life-saving process consists either in stopping oxidation altogether by immersing the eggs in a potassium cyanide solution or by depriving them of oxygen (Marshall). The reducing power of semen would offer a method of depriving the fertilized eggs of an excess of oxidation. Marshall states, "A spermatozoon should contain two substances, namely, a cytolysin and a substance inhibiting the initial cytolysis." The lytic enzyme of human semen may correspond to the cytolysin and the reducing system to the substance inhibiting the initial cytolysis.

These considerations show how complex the problem of sterility is. Not only are anatomic and physiologic factors to be considered but also biochemical. We have been able to gain some insight into a few of these biochemical factors and have demonstrated how one may be recognized clinically. Considering the great number of possibilities wherein the fertilization process may go astray, one wonders why sterility is not even more frequent than it is.

IV. SUMMARY

1. There is present in human semen a substance that dissolves human cervical mucus.

2. The properties of this lytic substance suggest that it is an enzyme.

3. Considerations are offered relating this substance to sterility and fertilization.

4. Semen has a strong reducing action on thionin and the possible significance of this reaction is discussed.

5. The reduction phenomenon of semen may have a bearing on the oxidative processes following fertilization.

6. Semen contains neither oxidase nor glutathione.

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THE ALLEGED SYNERGISM OF MAGNESIUM SULPHATE AND MORPHINE

A Further Communication

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A RECENT article by Gwathmey,[1] which he describes as a reply to an article of mine[2] on the alleged synergism of magnesium sulphate and morphine, places me under the embarrassing necessity of again discussing my work. I shall consider the subject briefly under three heads: (1) a recapitulation of the studies, (2) an examination of the reply, (3) suggestions for the further investigation of the problem.

RECAPITULATION OF STUDIES

Several years ago I desired to introduce studies of the ether-oil colonic method of inducing anesthesia into our laboratory courses in pharmacology in order that the whole subject of anesthesia might be more completely laid before the student. There was at that time no experimental arrangement available to us for routine laboratory work which satisfactorily demonstrated the part played by the several factors which contribute to success with this method. I therefore undertook a study of the subject upon dogs and was very pleased to observe the ease with which I could invariably induce surgical anesthesia in these animals under conditions identical with those employed in the human except for the fact that the initial dose of morphine had always to be proportionately larger. Completing the arrangement for the routine laboratory demonstration, I then undertook certain independent investigations of the subject. Being impressed by the small amount of ether employed in the method, I undertook to reduce this amount still further by availing myself of the depression induced by

the parenteral introduction of magnesium sulphate. Finding very early, however, certain evidence that the ether was already employed at its minimum effective dose or nearly so, I then directed my attention toward a reduction of the morphine. Here again I employed magnesium sulphate, this time for the synergistic effect that it is alleged to have upon morphine, which effect I firmly believed at that time to have been proved. My early failure, however, to find any evidence of this synergism caused me to turn to a more comprehensive study of the literature for assistance. I was surprised to find there no conclusive evidence whatever that this synergism occurs either in laboratory animals or in man. I therefore undertook a thorough study of the subject, a study in which I am still engaged. I was the more easily enabled to do this by reason of the fortunate circumstance that the colonic anesthesia experimental arrangement lent itself exceedingly well to the purpose. Here was an arrangement in which the coincident employment of certain factors, properly adjusted, always gave a certain result; to wit, morphine sulphate plus ether-oil by the colonic method gives surgical anesthesia. I then addressed myself to a careful study of the part played by each factor in bringing about this result in order that I might definitely fix the amount of sedation accomplished by the morphine. This was necessary if I wished to observe any increase of sedation which might be due to the addition of magnesium sulphate, since we are unable to describe as synergism the effect induced by the addition of one drug to another unless we have first studied the effect of the original drug alone.

As a result of these initial experiments I was able to determine very definitely the amount of sedation always accomplished by the morphine. Briefly summarized the evidence conclusively showed that:

1. When one ounce of a mixture of 75 per cent ether and 25 per cent olive oil per 20 pounds (9 kg.) body weight was introduced into the colon of dogs, one hour after the subcutaneous injection of 0.01 gm. morphine sulphate per kilo body weight, safe and satisfactory surgical anesthesia was induced and maintained for a little more than one hour. (The criteria for this state of anesthesia, employed in all cases, were described in the reports.)

2. When less than the above stated dose of ether-oil was employed, anesthesia was not induced even though the other factors were at their effective points.

3. When less than the above stated time interval was employed, anesthesia was not nearly so satisfactory even though the other factors were at their effective points.

4. When less than the above stated dose of morphine sulphate was employed, anesthesia was not induced even though the other factors were at their effective points. This effective dose of morphine was fractionated and it was shown that only beyond 0.0075 gm. per kilo did light anesthesia begin to appear, and that only when the full dose of 0.01 gm. per kilo was employed did the resultant anesthesia satisfy the criteria for the state used throughout.

Thus, it was shown that in a given experimental arrangement, a given amount of morphine always accomplished a certain amount of

sedation; namely, that amount which was always sufficient to enable the ether to overcome the animal. This was looked upon as establishing the definite sedative power of the morphine under these conditions, and was therefore utilized as the basis for subsequent attempts to raise this power by the addition of magnesium sulphate.

These attempts were comprised in three series of experiments. First, by testing the ability of the magnesium sulphate to raise the sedative power of the morphine in the following arrangement: effective dose of morphine plus magnesium sulphate, effective time interval, less than effective dose of ether-oil. Second, by testing the ability of the magnesium sulphate to raise the sedative power of the morphine in the following arrangement: less than effective dose of morphine, plus magnesium sulphate, effective time interval, effective dose of ether-oil. The dose of morphine was fractionated here in exactly the same way as it had been in the initial experiments in which the effective dose had been determined. Third, by testing the ability of the magnesium sulphate to raise the sedative power of the morphine in the following arrangement: effective dose of morphine plus magnesium sulphate, but the magnesium sulphate given one-half hour before the morphine, effective time interval, effective dose of ether-oil.

Whenever I encountered evidence of an increased sedative power of the morphine it was my intention to counteract the influence of the magnesium sulphate by employing its antagonist, calcium chloride. Had the increased sedation persisted, I should then have felt that I was dealing with a true case of synergism. The opportunity to employ this technic never arose, however, for in no instance was I able to observe such an increase; i.e., in all cases anesthesia was induced only when all factors were adjusted as had been shown to be necessary in the initial studies in which magnesium sulphate had not been employed. Also, a peculiar and still unexplained reaction manifested by the dogs in these experiments, enabled me quite unexpectedly to note that the analgesic power of the morphine was likewise not raised by the magnesium sulphate. Thus, all the dogs given magnesium sulphate began howling when the ether began to be absorbed from the colon, this howling quickly reaching agonal intensity and persisting until the ether-oil was washed out with tap water. In experiments performed outside this series it was easily shown that this reaction, which must have been due to pain, was caused by the coincident presence in the organism of magnesium sulphate and ether, the method of introducing the ether making no difference in the symptoms. Morphine was effective in overcoming this pain and always did so when it was given in that dose which had been previously shown to be its effective sedative dose. The presence of the magnesium sulphate did not enable smaller doses of morphine to overcome this pain; i.e., it

failed to raise the analgesic properties of the drug as it had also failed to raise its sedative power.

In the course of the studies one hundred and thirteen experiments were performed, employing fifty-one animals ranging in weight from 5 to 23.5 kg. Full accounts of the work and the results, briefly summarized above, were published[3] in due detail, together with my two conclusions, the first of which was that the alleged synergism did not occur in the dog.

Turning to the clinical literature, I then pointed out that my reasons for refusing to accept any of the evidence therein offered of the occurrence of this synergism in man were as follows: the failure of most observers to select such phenomena for modification by drug action as would easily lend themselves to sharply drawn comparisons; their disinclination to distinguish clearly between addition and true synergism, and, above all, their tendency to describe as synergism the overwhelming effect seen when abnormally large doses of either drug are given. My second conclusion was, then, that no satisfactory evidence had been brought forward to show that this synergism occurs in man.

In attempting to account for the persistent belief that this synergism does occur in man, in spite of the fact that there is no scientific evidence to prove it, I stated my opinion that it is due to the sincere conviction that the synergism must take place because of the essential nature of the two substances; i.e., the one an indifferent narcotic, the other an alkaloidal narcotic. I then showed, by reviewing in my pages the work of a number of independent investigators, that such predictions cannot be made and that only actual experimental results can be accepted as having any scientific value.

EXAMINATION OF THE REPLY

That which alone has enabled science to contribute to the welfare of our present day world is the fact that at once its aims, methods, and obligations are incorporated in its definition. Though capable of being phrased in many different ways, that definition must always be to the effect that science is an orderly arrangement and record of unbiased and accurate observations of phenomena, either with or without an attempt to explain it in terms of other phenomena similarly recorded. Any person engaging in scientific pursuits, whether as neophyte, teacher, or research worker, must early formulate his credo out of some such statement if he is to attain to understanding of the cause he espouses. Obviously it is of the very essence of the definition that science is a plastic thing, slowly growing by hewing away here and adding on there, the two processes being of equal value. Therefore it follows that anyone offering a sincere contribution must necessarily do so in the certain knowledge that he is but furnishing more

material for the chisel, finding his consolation in the secure faith that the new modeling will be done accurately and without bias. So growth proceeds.

I am led to make the above trite observations because it is my belief that now and then a reiteration of first principles is timely. I shall attempt to point out the lanes of attack along which I feel, therefore, that any legitimate scientific reply to my work must proceed.

1. The alleged synergism of magnesium sulphate and morphine is alone being considered. Therefore, any matter not germane to this subject can have no place in the discussion.

2. I have presented detailed accounts of certain investigations of the alleged synergism made by me upon animals, together with a record of my observations and the conclusions drawn therefrom. Issue can be taken with this work only when (a) it can be shown that exactly similar investigations have been made with entirely different results, or when (b) evidence is offered that the subject has been investigated upon animals using an entirely different experimental arrangement, with interpretations at variance with those made by me upon my own experimental arrangement. In either case, regardless of the issue, such work would be only stimulating to further investigations.

3. I have stated the opinion that this synergism has not been shown to occur in man. In controversion of this opinion any evidence offered must show that simple addition, or the use of abnormally large doses of either drug, or the preponderance of the action of one drug over the other, is not being mistaken for synergism.

4. I have contended that prediction of synergism by reason of the nature of the drugs concerned cannot be made. To upset this contention it must be shown that Bürgi's "law," as originally stated and many times modified, is valid.

That Gwathmey has failed to reply convincingly under any of these heads can be shown:

1. The title of his paper is "The Synergism of Magnesium Sulphate and Morphine and the Synergism of Magnesium Sulphate and Ether." Only the alleged synergism of magnesium sulphate and morphine having been considered by me, all that he has to say regarding the synergism of magnesium sulphate and ether, comprising a very large part of his paper, does not apply to the discussion. Likewise, the introduction of a discussion of the combined use of procaine, magnesium sulphate, and morphine, since it throws no light upon the mooted point, has no place.

2. As evidence of the occurrence of this alleged synergism in animals he says: "The synergism between magnesium sulphate and morphine was first observed in the laboratory by E. J. Pellini, of the

University and Bellevue Hospital Medical College, and immediately applied in the clinic, where its value was proved beyond question by trained observers." As a reference for study of this animal work he cites a paper of his own. I have already discussed that paper in one of my previous articles.[3] I take the liberty of quoting what I said at that time: "He (Gwathmey) states that this combination was first suggested to him by Pellini, and from the work they performed together, Gwathmey offers the following as his sole experimental evidence:

> "A sufficient number of animal experiments was conducted to prove that one-eighth grain of morphine in 2 c.c. of a 25 per cent solution of chemically pure and sterilized magnesium sulphate, given hypodermically and repeated twice at half-hour intervals, analgised an animal sufficiently for the full force of an artery clamp to be placed anywhere on the skin without being noticed by the subject. The controlled animal, with the same dosage of morphine, was not analgised to anything like this degree."

The size of the animals used is not mentioned, nor is the number of experiments performed stated. Also, to accept the mere statement that the dogs given morphine alone were "not analgised to anything like this degree" as one having any very real scientific value is impossible, especially as it is well known that dogs become markedly insensitive to pinching on even very small doses of morphine, though they will at the same time resist cutting and also show signs of heightened activity of the more superficial reflexes, such as to light and sound.

I feel that this, the only evidence of animal work that he offers, has no scientific value whatever.

3. As evidence that this alleged synergism occurs in man he offers three tables. Table I furnishes data of a case in which the patient experienced greater relief from pain when given morphine plus magnesium sulphate than when given morphine alone. This mere fact does not, however, constitute proof that simple addition did not bring about this result; indeed, the second longest period of relief was experienced in one of the two instances only in which magnesium sulphate alone was used. Tables II and III comprise lists of cases in which the time before postoperative sedative was shown to be longer when morphine plus magnesium sulphate was used preoperatively than when morphine was used alone. Here again there is no evidence of synergism. Both experimental and clinical literature offer abundant proofs that magnesium sulphate is a powerful sedative, which evidence I have never sought to question; in fact, I have published certain observations of the powerful, depressing effect it has upon dogs. However, that the salt has the ability to raise specifically the sedative power of morphine, I do hold to be not proved.

4. The subject of the prediction of synergism treated by me was not touched upon in the reply. This was, of course, not obligatory.

SUGGESTIONS FOR THE FURTHER INVESTIGATION OF THE PROBLEM

The various experimental arrangements which might be utilized for study of this subject in the specialized laboratory present themselves so easily to the mind that they need not be reviewed here. It is hoped that some of us in this, or some other laboratory, will have something to contribute toward the further elucidation of the problem in the near future.

As to its clinical investigation along scientific lines I take the liberty of briefly suggesting a plan which I am not in a position to put into operation myself. To wit: a large series of patients to be treated with morphine alone; a similar series with magnesium sulphate alone; a third series with morphine plus magnesium sulphate, neither of the drugs to be used in larger amount than when used alone. If increased sedation is noted in this third series, the effect of the magnesium sulphate to be removed by its antagonist, calcium chloride; persistence of the increased sedation might then be looked upon as evidence of synergism. Work of this nature has been done upon animals by Mansfeld and Hamberger,[4] and I believe that it would be quite feasible to employ the method in the clinic.

CONCLUSIONS

I wish only to repeat my conclusions as stated in the last of my papers on this subject:

1. It has been shown in rabbits (Issekutz) and in dogs (this paper) that the alleged synergism of magnesium sulphate and morphine does not take place.

2. No satisfactory evidence has been brought forward to show that this synergism does occur in man.

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638 FOURTH STREET.

OVARIAN DYSFUNCTION DEPENDENT ON ABNORMALITIES OF THE DUCTLESS GLANDS*

By Barton Cooke Hirst, M.D., Philadelphia, Pa.

IN CHOOSING a subject for presentation to this Society, I have been influenced by two considerations: first, the problem that perplexes me most in my practice today and secondly, the expectation of receiving more light upon it by the interchange of views and experiences from the members of this body. The dysfunctions of the ovary due to anomalies of endocrine secretion is, I think, as complex, as fascinating a field for investigation, experimentation, and clinical observation as any that medicine presents today. The ultimate solution of this problem, by piecing together bits of information slowly and laboriously obtained, promises relief to a large and increasing number of women as well as relieving physicians from the humiliating sense of futility that has heretofore discouraged us in our efforts to cure such cases.

It is unnecessary to remind such an audience of the pioneer work of Sajous, the investigations of Blair-Bell, the experiments of Stockard, the observations of Papanicoloau, Frank, Allen, Doisy, Zondek, and many others. It suffices to marshall together the facts established at present by many painstaking investigators.

For the normal performance of their cyclical functions, the female sex organs depend on a hormone secreted first by the theca cells of the graafian follicle, of connective tissue origin, and next by the epithelial cells of the granulosa as the theca cells atrophy. It is present in greatest concentration and potency in the developmental stage of corpus luteum growth and entirely absent in its retrograde stage in the nonpregnant female. It is not found anywhere else in the ovary; not in the capsule, nor in the primoidial cells or stroma. The same hormone is found in the placenta, whether stored or produced there is not known. This hormone known as the female sex hormone is also produced during pregnancy and is found in parts of the ovary then from which it is absent in nonpregnant females—in atretic follicles and in the corpus luteum in its later development.

The sex hormone is found in the blood stream in varying amounts during the menstrual cycle, most during the premenstrual congestion and least during the menstrual flow (Frank) when, however, it is found in much larger amounts in the menstrual blood than it is ever present in the blood stream. It is also found in the urine.

*Read before the Chicago Gynecological Society, March 18, 1927.

The female sex hormone alone of all the endocrine and glandular secretions of the body will induce an estrus in a spayed rodent (mouse or rat); and it will bring about a premature puberty with estrus in immature animals. The hormone of the anterior lobe of the pituitary gland and the decidua vera will also hasten puberty (Aschheim), perhaps in the latter case because it may contain the sex hormone. The secretion from the anterior lobe of the pituitary gland, however, will not establish an estrus in a spayed animal. It does, however, induce an acute congestion of the ovary, if present, and a hyperplasia of theca cells and thus brings about an increased secretion of the sex hormone, but in a spayed animal it has no effect.

Administered by the mouth the sex hormone is positive in its action, but according to Loewe, twenty times the dose is required as contrasted with hypodermic administration. The dose, at least among the rodents, must be proportionate to the weight of the animal. Thus, one mouse unit, the smallest quantity that will produce an estrus in a spayed mouse, is only one-fifth the quantity required for a rat and one-fifteenth that required for a guinea pig. If this proportion holds good for the human female, three thousand mouse units would be needed for hypodermic use and sixty thousand units for administration by the mouth. Loewe, in an investigation of the commercial products in the shape of tablets, could not find in any of them more than a fraction of a mouse unit of the sex hormone, so that any effect on the human system would require the consumption at one dose of several thousand of them! It would seem, however, that this proportion does not hold good for the human female, for Loewe found that 40-100 c.c. of blood from a healthy woman of childbearing age contained one mouse unit of hormone and that therefore the whole blood stream would contain 40-150 mouse units. On the contrary, Bugbee and Simond found that in the rat the dose must be proportionate to the weight.

Curiously enough Loewe found in the blood from the umbilical cord one unit to 15 c.c. of blood, a proportion probably due to the quantity stored or produced in the placenta.

So much may be stated without fear of contradiction. These facts are of the utmost importance to a comprehension of the physiology of sex and of reproduction. They are also of the greatest interest to the clinician, for they suggest possibilities of therapeusis hitherto beyond our reach.

One more statement of fact may be added, though it is ignored by some of the foremost modern investigators who are concentrating their attention on the sex hormone. Stockard and Papanicoloau declare that if an extract from the corpus luteum in its ultimate form is injected in guinea pigs, the estrus is delayed three days, and if the injection is repeated, the sexual function is abrogated altogether.

Seitz and Wintz isolated two antagonistic hormones from the corpus luteum, one a stimulating substance, probably the sex hormone; the other an inhibiting agent, checking the menstrual cycle and the uterine bleeding following its culmination. A commercial firm has on the market tablets which are said to contain these substances. A few clinical experiences of ours would seem to substantiate this claim, especially one case in which a nine months' amenorrhea yielded to treatment only after the stimulating tablet was added to electrical stimulation of the pelvic organs and the injection of the sex hormone; but it is only fair to state that the sex hormone was very weak in units compared with a product which we are now promised after some two years' work in the clinical application of the hormone therapy in collaboration with a commercial firm (Parke, Davis and Company), who supplied us with the material for clinical application while energetically endeavoring to increase its potency.

A word here as to the pharmacologic aspect of the subject: Loewe, in a meeting of the Berlin Gynäcological and Obstetrical Society in January, 1926, stated that the best he could do in the preparation of a tablet for ingestion by the mouth was to make it of a strength of ten mouse units. The firm referred to above promises us a product for hypodermic use of twenty-five to thirty-five rat units, perhaps a little more. If Loewe's statement of the blood content of forty to one hundred and fifty mouse units is correct, this preparation would seem to promise results, such as we have never been able to obtain before. To prepare a solution of such potency, it has been necessary to obtain the hormones from the placenta. The preparation from the graafian follicles demanded such a large gland consumption as to be impracticable.

After a brief review of established facts which may be said to be incontrovertible, there is room for speculation in regard to a function of the ovary not demonstrated as yet by scientific laboratory research but suggested by clinical empyricism.

The connective-tissue stroma of the ovary is usually dismissed as having no function whatever, and yet the theca cells of connective-tissue origin undoubtedly secrete the sex hormone. It would not be surprising, therefore, to find the ovarian stroma producing a hormone of physiologic activity. We are all familiar with a peculiar type of inexplicable menorrhagia and metrorrhagia in young nulliparous women and virgins, in which the usual causes can be excluded. There is no syphilis, no hypertension, no abnormality in clotting time, no displacement or other pelvic abnormality, no chronic malaria, no valvular heart defect. Uterine astringents are useless, and curettage has no effect. Some of these cases have been cured in my practice by ovarian residue when everything else has failed. Is it not possible that the cells of the stroma have a restraining effect upon the development

of the endometrium, overstimulated perhaps by an excess of sex hormone, or unchecked by a deficient development in the later stages of corpus luteum formation, a condition found in so-called cystic ovaries in which the graafian follicles never reach their full development and fail to produce a typical corpus luteum?

The main problem that I had in mind for discussion is the agents at our command and choice of treatment in cases of scanty and infrequent menstruation or complete amenorrhea and the accompanying sterility, for which so many patients are consulting us.

The three specific agents at our command that may restore or initiate a normal sex physiology are the sex hormone, electrical stimulation of the pelvic organs, and the stimulating dose of the x-ray.

With the first two I have had experience, but I have much more to learn. With the last I have no personal experience, for I have felt reluctant to recommend it until the radical difference of opinion among roentgenologists is reconciled. I hear from some of them that the x-ray is always destructive to the sex glands, but Stockard's experiments on guinea pigs would seem to refute this statement, and I have been shown some convincing cases and statistics, especially in the Mt. Sinai Hospital in New York, that support Stockard's view. German literature contains many affirmative statements as to the stimulating dose on the ovary of the roentgen rays, and Professor Werner, of Vienna, claims that a stimulating irradiation of the hypophysis may supplant the application of the x-ray to the ovary.

Roentgenologists must settle these conflicting claims among themselves, but it looks as though we gynecologists must in time avail ourselves of this treatment in selected cases. Excluding this agent for the present, there is left to be considered the use of the sex hormone and electrical stimulation.

My experience with sex hormone began twenty-one years ago when, in collaboration with the late Professor Allen Smith, I prepared a glycerin extract from the human corpus luteum and injected it in a few women with some positive results. One remarkable case was that of a patient with acute suppurative salpingitis from whom both tubes and ovaries were removed, according to the record taken in operating room at the conclusion of the operation. This woman returned with the symptoms of the precipitate menopause. She received one hypodermic injection of the corpus luteum extract and was lost sight of until some three months later when she returned pregnant. There must have been a scrap of ovarian tissue left which was stimulated to ovular production by the sex hormone.

These experiments of mine were then intermitted on account of the difficulty of procuring sufficient material to work with. When commercial firms began to put on the market various combinations of endocrine products for mouth administration, I tried them extensively

in many combinations, but with the unsatisfactory results we have all doubtless experienced. Stimulated by Stockard's experiments, I secured from Parke, Davis and Company ampules of the sex hormone, which were also distributed to members of my Staff, Dr. John C. Hirst, 2nd, and Dr. Andrussier. During the past year or more, this preparation has been used in some forty cases. Dr. J. C. Hirst has reported recently to the Philadelphia Obstetrical Society the results in his series, excluding some early cases, as the first ampules contained only one rat unit, and some of the patients failed to appear regularly. The results were in some instances quite striking, in others negative. My own experience was the same. On the whole our results were much like those of Frank, Pratt, Allen, and others. There was nothing comparable with the exact and invariable results secured in mice, rats, guinea pigs, and monkeys. There seems no rational explanation for this fact except the dosage. If Loewe's calculations are correct and if weight alone dictates the dose, women should receive three thousand mouse units or six hundred rat units which, as far as I know, they have never received. Allowing for the fact that this proportion may not be necessary in the human female, the dose heretofore employed has been so minute compared with the woman's weight it is strange that any results at all have been secured. It would appear, therefore, that at least one hundred rat units might be the initial dose, to be increased steadily until something like the invariable effects in the lower animals appear. If we are supplied with ampules containing, as I am assured, twenty-five to thirty-five rat units, such doses become practicable. The best manner of administration must be determined by clinical observation. The convenience of the patient must be considered. It will be difficult to find patients who will submit to several injections a day, as they are given to the rat,—three injections at four hour intervals,—and still more difficult to make them submit to this treatment daily over a considerable space of time. Fortunately this will not be necessary. Loewe, whose study of this subject from the pharmacologic point of view is valuable, points out that the sex hormone is stable in the system; that the effect of the injections appears in mice and rats at the end of seventy-two hours, and that, therefore, the injections in human beings need not be given more frequently than every other day. Consequently, I cannot see why we should not give a single massive dose, increasing, if our experience shows it to be necessary, until the physiologic result is secured. I intend to act on this assumption in the future, and I hope those of this audience who are interested in the subject may try a similar plan, so that a collective investigation will shortly demonstrate whether our expectation of the success of this treatment is justified or not. At present I have four women under treatment with respectively 25, 50, 75 and 100 rat units as the initial dose.

In regard to the electrical stimulation of the pelvic organs, I feel myself on much surer ground. I have employed this agent for more than fifteen years and have secured results in some cases not, I believe, to be obtained in any other way. With the negative pole, in the shape of a metal ball on an insulated handle, resting against the cervix and a large sponge pad on the abdomen, galvanism (about 12 milliamperes), faradism, and the sinusoidal current can be applied. While there is nothing specific about this treatment as a physiotherapy, its value in other regions on ill-developed or atrophic muscles and as a stimulant of circulation, nutrition, and a corrective of apathetic function is universally recognized.

My best results, I must confess, have been in the cases of superinvolution, but they have also been encouraging in primary amenorrhea and lack of development, except in extreme cases that are obviously hopeless. Incidentally this treatment will cure permanently the most obstinate cases of constipation and a hypertension dependent on intestinal toxemia. Some of the results of this treatment have been reported to the American Electro-Therapeutic Association.

Finally, our increasing knowledge of female sex psysiology and the utilization of this knowledge in the treatment of its anomalies impresses on us the necessity of a more accurate differential diagnosis. We feel the need of distinguishing between the amenorrhea of an atrophic endometrium in a shrunken or ill-developed uterus with ovaries whose function is normal or simply held in abeyance but not abrogated and ovaries primarily at fault. Other questions suggest themselves, such as the determination of doubtful sex in pseudohermaphrodites.

Clinical laboratories in connection with our large hospitals must be prepared to meet this demand. We should be able to ask for a report of the proportion of sex hormone in the blood, urine, menstrual blood, and the blood of the umbilical cord.

In a retrospect of the past, a survey of the present, and a glimpse into the future, it is evident we are on the threshold of an addition to our therapeutic power equally welcome to ourselves and to our patients.

(For discussion, see page 121.)

1821 SPRUCE STREET.

RUPTURE OF THE UTERUS IN THE SCAR OF A PREVIOUS CESAREAN SECTION OCCURRING TWICE IN THE SAME PATIENT WITHIN ONE YEAR*

By Maurice J. Gelpi, M.D., New Orleans, La.

ALL acute abdominal emergencies have a certain fascination for the surgeon, but few, if any, furnish a source of greater interest than rupture of the uterus following cesarean section. I have witnessed this catastrophe only three times, but the accident occurred twice in the same patient, which makes the case of sufficient interest to warrant its presentation.

CASE REPORT

Mrs. F. S., a white woman, aged 27, was admitted to Charity Hospital by ambulance December 25, 1919. At the time of admission she was cold, pale and clammy, her pulse was 140, and she complained of severe abdominal pain. Dr. H. L. Zengel, her attendant, had made a diagnosis of uterine rupture, so that preparations had been made for infusion and for immediate operation, and not a moment of time was lost on her arrival in the institution. Immediate laparotomy, after infusion, revealed a rupture of the uterus in the scar of a previous cesarean operation. This scar was in the fundus and longitudinal, about three and a half inches long, and was ruptured throughout its length. The placenta protruded through the rupture, and the abdominal cavity was filled with free blood and clots. The clots were quickly removed, but no attempt was made to remove the remaining blood and serum. After the removal of a perfectly formed, dead fetus, and the placenta and membranes, the old uterine scar was excised and the uterine wound rapidly sutured. Number two chromic catgut interrupted sutures were first inserted about three-quarters of an inch apart, and these were supplemented by a single continuous suture of number two chromic catgut. (Since that time I have been suturing the uterus after cesarean section in three tiers.) The abdominal wall was closed as usual in layers. No other procedure was considered at the time because of the serious condition of the patient. In about seventy-two hours the primary effects of shock and hemorrhage gradually disappeared, and her recovery was excellent. She was discharged in good condition January 13, 1920.

Her previous history, which was secured after operation, revealed the fact that she had been married six years and had had her first child normally at term five years before admission. Two and a half years later a second child was delivered at seven months by cesarean section, by Dr. A. O. Hoefeld, the indication apparently being placenta previa. The child, though premature, was normal, and lived. The mother, however, "broke her stitches," to quote her own description, and had to be resutured. The third pregnancy was quite normal until Christmas day, 1919, the day of her admission to the hospital, when, after she had carried her child for five squares, straddling her abdomen, she was suddenly seized with violent, acute abdominal pain, followed by air hunger, thirst and weakness. It was at this stage that Dr. Zengel saw the patient, diagnosed her condition, and sent her into the hospital, with the results already described.

*Read at a meeting of the New Orleans Gynecological and Obstetrical Society, April 7, 1927.

On December 16, 1920, less than a year after the first rupture, I was informed by telephone that this same patient, then some seven months pregnant, had developed precisely the same symptoms as she had previously experienced. She was immediately brought to the hospital in the ambulance, and physical examination revealed exactly the same findings and symptoms as on her first admission, though her pulse was only 120 and her general condition was not so critical. Immediate laparotomy disclosed a rent about a half inch wide between the edges of the second cesarean scar. The whole scar was thinned out and very much attenuated, so much so that when later the uterine wall was held up to the light, it was actually translucent. The peritoneum still covered most of the rupture, so that the membranes were found intact. The placenta was situated posteriorly, and was not in contact with the scar at any point. A Porro operation was done, a normal, living child was extracted, and both mother and baby made an uneventful recovery.

I have recently been informed that mother and child are both living and well, and, *mirabile dictu*, exceedingly grateful.

(For discussion, see page 118.)

CHAILLE BUILDING.

HERNIA FUNICULI UMBILICALIS, WITH REPORT OF THREE CASES*

BY A. F. HEBERT, M.D., NEW ORLEANS, LA.

IT HAS been my good fortune during the past ten years to have under my observation three cases of congenital hernia of the cord, and after careful search of the literature, French, German, Italian and Spanish, as well as English, I have found but one physician who had treated a larger number, namely, four.

W. S. MacDonald reviewed the literature up to 1890 and found eighteen cases which had been operated upon, with sixteen recoveries and two deaths. These, however, were all of the small variety, with the intestines the only contents of the sac. He found twelve cases which had been treated expectantly, with three recoveries and nine deaths. He himself had had one case under his observation, which he had operated upon six hours after birth, the contents of the hernia being the ileum, ascending colon, cecum and appendix.

Samuel C. Benedict in 1892 reported one case in a ten-pound child, with the liver, spleen and bowels in the hernial sac. Operation was done fifty-three hours after birth, but the results are not stated.

G. C. Stewart in 1904 reported one case in an otherwise normal male child, the hernia being the size of an apple, and containing the liver and bowels. Operation was done fifteen days later by Dr. Griffith.

George W. Cutler in 1919 reported three cases, one of which he operated upon twenty-four hours after birth.

Frederick G. Dyas in 1920 reported one case operated upon eight hours after birth. The contents of the sac were only the intestines. The child lived two days and died of congenital atresia of the bowels.

Edgar G. Mathis reported two cases. The first, one of twins, was a normal sized male child, who was operated upon forty hours after birth. The sac contained about

*Read at a meeting of the New Orleans Gynecological and Obstetrical Society, April 7, 1927.

half of the liver, and death ensued in eighteen hours. The second was a seven-pound male child, who recovered through expectant treatment. The sac contained only intestines, and after the cord dropped, granulation took place over the hernial opening.

Ricardo Carnelli, Director of the Civil Hospital of Modeliana of North Italy, reported the case of a girl, delivered normally and operated upon five hours after birth, who lived five days. The liver and intestines were in the sac.

Frederick C. Pybus reported one case in which the hernia was the size of a chicken egg and extrophy of the bladder was present. Operation was done six hours after birth, and death ensued in seven days.

D. T. Cannon reported a case operated upon six hours after birth, in which the tumor was the size of a large pear. The child lived six months and died eventually of marasmus, largely through parental carelessness.

H. Fowerlin and D. P. Bade reported the case of a healthy female weighing nine pounds, with a hernia the size of a chicken egg. Operation was done nine hours after birth, the sac containing two loops of bowel together with the cecum. Chloroform was administered for an hour.

Reifferscheid of the Woman's Clinic at Göttingen reported the case of a four and a half pound child, operated upon eight hours after birth. The hernia was quite large and contained the liver and intestines. The wound did not close for twenty-five days and the child was finally discharged with a large postoperative hernia.

Unfortunately, the various case reports are not all given in detail, and comparison of the conditions found, the procedures and the results is obviously impossible.

Malgaine was the first to study these deformities, and to emphasize the fact that they were not true herniae, since the viscera had never entered the abdominal cavity. Ruysch in 1691 called attention also to the fact that the umbilicus is not developed in these cases. Different opinions are held as to the etiology. Cruveilhier believes the cause to be pressure in the abdomen of the fetus due to faulty position. Scarpa considers it to be traction on the cord, because of winding about the fetal body. Ahlfred considers it to be constant pulling of the vitelline duct on the intestines in the root of the umbilical cord. St. Hilaire believes that accidental bands of adhesions hold the viscera out of the abdomen.

The condition is quite infrequent. In the last 8,410 obstetric cases handled at Touro Infirmary there were but two instances; one child was operated upon with recovery, the other died shortly after birth. There was no report of such a condition in the last 10,995 cases at Charity Hospital. At the Long Island College Hospital two instances are reported in 7,200 deliveries; one of these was so extensive that operation could not be considered; the other child was operated upon, but died in twenty-four hours. Sixteen cases are reported in 29,780 deliveries at the New York Lying-In Hospital. One of these was operated upon and death followed in a few hours. Watson states the frequency of congenital umbilical hernia to be about one in ten thousand, and the collected statistics would probably bear him out.

The diagnosis is usually evident. A tumor mass is apparent on the abdomen immediately after delivery, the size depending upon the contents, and the only other conditions to be considered are hydrocele

of the umbilical cord and urinary diverticulum. In the smaller hernias strapping gives good results, but surgery is the only possible treatment in the graver types.

CASE REPORTS

CASE 1.—Baby K., born April 18, 1918, male, eight pounds, six ounces, normally delivered of a multiparous mother. A mass about the size of a small orange was apparent at the umbilicus, covered with amnion, Wharton jelly and peritoneum, with coils of intestines definitely palpable. Several attempts at reduction were made, but it was obvious that the intestines could not thus be restrained. About forty-five minutes after birth operation was done by Dr. William Kohlman under ether anesthesia. An incision was made through the amnion, Wharton jelly and peritoneum, opening into the cavity, and revealing the presence outside the cavity of a loop of small bowel with the cecum and appendix. No adhesions were present. The amnion and peritoneum were cut at the edge of the skin, and closure was done in tiers. The recovery was uneventful.

CASE 2.—Baby H., born November 22, 1923, of a primiparous mother; weight six pounds. Forty-five minutes after birth, when I first saw the child, a dark colored, oblong mass, about three by two inches, was present at the umbilicus. Under ether anesthesia an incision was made through the amnion, Wharton jelly and peritoneum, the peritoneum being separated from the bowel with some difficulty because adhesions had already formed. The bowel was quite dark, and there was a plastic exudate between the coils. The condition was obviously hopeless, since gangrene had already set in, and the amount of bowel involved made resection an impossible procedure. The contents of the sac were rapidly reduced and closure done in tiers. The child lived about fifteen hours.

CASE 3.—Baby J, born July 21, 1926. The child was premature, weighing but five pounds, and I saw her within ten minutes after birth. A large mass, the size of an orange, was present over the anterior surface of the abdomen, extending from the xyphoid process downwards. The upper half of the mass was quite dark and hard, the lower part was soft, and palpation showed it to contain bowel. About twenty minutes after birth operation was done. Under ether anesthesia an incision was made from the xyphoid process to the lower border of the mass, through the amnion, Wharton jelly and peritoneum. At first the knife encountered a hard substance, which proved to be the liver. In the course of separating it from the peritoneum, another obstruction was met, the falciform ligament, and with the scissors this band was cut to the edge of the skin. After the liver had been completely separated from the sac, it was found to be torn in two places, repair being done with U sutures. When the liver was thus freed and the bowel was ready to be replaced in the abdomen, the amnion and peritoneum were cut at the edge of the skin, leaving an opening in the interior abdominal wall about four inches long and two and a half inches wide. Closure was done in tiers, using chromic catgut number one for the peritoneum and fascia, and plain double 0 for the skin. Twice during the operation the child stopped breathing, and was revived by artificial respiration. For three days it vomited everything given it, and finally, as a last resort, it was permitted to nurse at the breast. From that time recovery was uneventful, and it is now a normal, healthy baby, having been examined last on July 21, 1927.

(For discussion, see page 116.)

MAISON BLANCHE BUILDING.

A NEW STYLE FUNNEL FOR USE WITH THE ELECTRIC OR KIETH WATER POWER BREAST PUMP

By F. P. McNalley, M.D., F.A.C.S., St. Louis, Mo.

(From the Department of Obstetrics of Washington University School of Medicine and Barnes Hospital)

THE electric and water power (Kieth) breast pumps for use in the hospital and home have provided us with, by far, the most satisfactory means of emptying the nursing breast devised up to the present time. Their short-comings lie only in the funnel. The chief difficulty with the funnel supplied with the Abt pump is that the nipple is drawn down into the stem of the funnel and occludes the ducts. This happens immediately in the small flabby breast, and in most breasts after the pump has been used for a while. Kieth has corrected this defect to a certain extent by enlarging the small end of the funnel just before it reaches the stem. However, there are many nipples that are sucked past this enlargement into the stem.

Another difficulty noted only in the firm, hemispheric breast is that instead of being pulled too far into the funnel, it is only pulled in part way and the portion at the level of, or just above, the areola is compressed, shutting off the ducts and stopping the flow of milk.

In an attempt to overcome these difficulties, various sizes and shapes of tapered funnels were tried, without success. Finally, it seemed reasonable that since nursing by the baby was entirely on the nipple, any attempt to imitate the maternal process should be devoted to this area. With this in mind the present funnel was designed, and after considerable use seems to be an improvement over the other types. Up to the present time it has pumped all breasts satisfactorily. Its advantages are that its use is more comfortable to the patient, and that it empties the breast faster and more completely.

The Henry Heil Chemical Company of St. Louis has had some made of ordinary glass which are now in use. If the breakage is too great, pyrex glass will be substituted.

I wish to express my appreciation to Mr. Varney of the Department of Bacteriology, for his cooperation in making many of the experimental funnels.

Society Transactions

AMERICAN GYNECOLOGICAL SOCIETY

FIFTY-SECOND ANNUAL MEETING

HOT SPRINGS, VA., MAY 23, 24 and 25, 1927

(Concluded from the December issue.)

DR. W. C. DANFORTH, Evanston, Ill., and DR. B. C. CORBUS, Chicago, Ill. (by invitation), presented a paper entitled **Pyelitis in Pregnancy**. (For original article see October, 1927, issue, page 544.)

DISCUSSION

DR. L. A. CALKINS, UNIVERSITY, VA.—Pyelitis during pregnancy is a very important problem with us. We have diagnosed pyelitis 32 times in the last 650 pregnancies coming into our clinic, making an incidence of about 5 per cent. Fourteen of these presented clinical symptoms during pregnancy, and 18 in the first few days after delivery; the postpartum cases usually showed symptoms within twenty-four to seventy-two hours after delivery. The fact that so many patients with pyelitis after delivery improve after they are placed in a recumbent position, and that those who have symptoms previous to labor improve so markedly and so promptly after delivery, is very suggestive. That there is something more than pregnancy seems beyond reasonable doubt. The only suggestion that I have to offer is that possibly a patient may not have pathologic alterations in her upper urinary tract, but that the normal anatomic constrictions of the ureter (usually the lower two of the three, the one at the pelvic brim or the one at the ureteral bladder junction) may be affected by the pregnancy with its normal pelvic congestion, involving all the organs in the pelvis, and thereby become sufficiently tight to produce obstruction in the upper urinary tract and bring about a possible infection.

It was interesting to note that of our 14 cases presenting clinical symptoms during pregnancy, 12 required local treatment of the type referred to by Dr. Danforth; whereas of the 18 showing clinical symptoms after delivery only one required local treatment. The other 17 responded to the general measures usually employed.

DR. ALFRED C. BECK, BROOKLYN, N. Y.—Our pregnant patients with pyelitis divide themselves into two groups. In the one, the patient appears in our clinic within a day or two after the onset of symptoms. Rest in bed, the Trendelenburg posture, requiring the patient to lie on the left side, forced fluids and alkalies, as a rule, result in prompt relief of the symptoms. We do not find any pathologic changes later in these cases. The patients that come to us, however, after the symptoms have existed for some time do not all respond to this treatment. Some of them require catheterization, and in our clinic we prefer to resort to drainage by catheter rather than lavage.

DR. J. HOFBAUER, BALTIMORE, MD.—I desire to present to the Society a brief report of the work done in the Obstetrical Department of the Johns Hopkins University on the subject of pyelitis in pregnancy, and to illustrate our findings by a number of lantern slides.

The present correlated study is an attempt to answer the following questions:

1. Why does the ureter undergo dilatation so frequently in pregnant women, and can the etiologic factor be established as a demonstrable obstruction in the urinary tract?

2. Is an association of bacteriuria with urinary stasis sufficient to produce an inflammation of the renal pelvis, or must some additional predisposing factor be considered, such as a lowering of local or general tissue resistance?

3. Does the infection of the ureter and the renal pelvis interfere with the process of restoration of the anatomy and function of these organs to the status *qus ante?*

4. Can certain new ideas be derived from this study with regard to the proper treatment of the condition?

The results of our investigations clearly show that the pelvic portion of the ureter during pregnancy undergoes a definite hypertrophy, and that this hypertrophy is most marked in the intramural and juxtavesical portion, while in the abdominal portion of the ureter, only a slight increase of the fibers is noticeable. Histologic examination bears out the point that both the muscle bundle and the connective tissue participate in the hypertrophy of the pelvic ureter, and particularly that the connective tissue, due to the abundant formation of new fibers, assumes a rather dense appearance. The ureteral wall as a whole presents a rather compact structure. In the juxtavesical portion of the ureter, in addition to the structural changes just mentioned, a very considerable hypertrophy of the ureteral sheath can be seen. In addition to these factors which result in a narrowing of the ureteral lumen, a more or less pronounced congestion of the mucosa may further narrow the lumen. In the area of the trigonum, a marked hypertrophy of its constituents,—muscle, connective tissue, and elastic fibers,—is a characteristic feature. This hypertrophy accounts for the clinical phenomenon that on cystoscopic examination the trigonum as a whole and the interureteral ridge in particular, appear more elevated and protuberant than in the nonpregnant woman. And for our present consideration this fact is of special interest, since of late such changes in the trigonum have been recognized as an essential factor in producing both a shallow cavity behind the interureteral ridge and a pronounced urinary obstruction. This factor affords an explanation for the frequent occurrence in pregnant women of the retention of several ounces of residual urine, an observation made first by A. C. Curtis.

Asymptomatic bacteriuria is not uncommon during pregnancy. The bacteria are excreted from the blood stream through the kidneys and the liver. The possibility of an ascending infection, however, may be considered in certain cases when the intravesical portion of the ureter has undergone to a high degree the structural changes outlined above, and the ureter has become converted from a collapsible into a rigid tube with a subsequent alteration of its valve-like arrangement in the ureteral orifices, as is sometimes seen on direct cystoscopic examination.

To set up inflammation in the renal pelvis, the local resistance of the tissues must be lowered or the general resistance of the organism must reach a low level. It can be shown that within the connective tissue of the renal pelvis there develops in pregnant women, in response to increased intrapelvic pressure, an accumulation of highly phagocytic cells— quite similar to the defense mechanism in the parametrium during labor. Pelvic overdistension spreads open this barrier, and the pelvic contents pass through these breaches into the venous capillary network of the calices,—"pyelovenous backflow,"—followed by the clinical symptoms of an acute attack. The study of the opsonic index in fifty normal women in various months of pregnancy showed that in about 10 per cent there could be demonstrated a marked lowering, as proved against three different strains of Bacterium coli. This observation tallies with the statement made by Koessler several years ago that during pregnancy there occurs a marked lowering of the opsonic index of the blood toward the tubercle bacillus.

Twenty-seven cases of pyelitis,—nine in which pyelitis developed during the puerperum,—were studied from four weeks to two years after the termination of pregnancy. Pyelograms showed considerable dilatation of the ureter in nine cases. Persistence of Bacillus coli in the urine obtained by ureteral catheterization, was found in seven out of fifteen cases, in which the organism was obtained at the time of the attack of pyelitis; persistent albuminuria and a large number of pus cells were found in two cases respectively.

One must conclude from these findings that termination of pregnancy merely renders the patient asymptomatic. With the subsidence of the classical symptoms, our treatment is not at its end,—indeed the real treatment must now begin.

If we succeed in conveying a clear conception of the etiologic factors operative in pyelitis of pregnancy, the course to adopt, in addition to the current treatment, is to restore, if possible, the efficiency of the atonic ureter; to increase the bactericidal power of the blood and the tissues, to limit the absorption of bacteria by changing the intestinal flora.

The administration of repeated small doses of pituitary extract answers several purposes: It increases both the tone and the automatic contractions of the ureter. It stimulates the elaboration of antibodies, particularly, when combined with infusions of a hypertonic glucose-solution, it exhibits a specific antiphlogistic action, and relieves ureteral congestion.

Lactose is known as the most effective carbohydrate in checking intestinal putrefaction. Calcium lactate has a similar effect. On account of the possibility of renal involvement no antiseptic drug should be used in the treatment of pyelitis in pregnancy.

DR. REUBEN PETERSON, ANN ARBOR, MICH.—In twenty-two cases of pyelitis in pregnancy hastily gathered together for this meeting, I find that there was very little preceding genitourinary disturbance. In fact, there were only two that gave a history of previous pyelitis, although in two the histories were doubtful. The symptoms began about the fifth or sixth month of pregnancy. Whether this is due to pressure of the uterus on the ureters or whether it is due to other causes as has just been brought out in the paper, I do not know. In one case, symptoms started at three months, although here there was a previous history of pyelitis. In ten of the patients, cystoscopy was practiced, and the passage of renal catheters showed pus from both ureters. In two the renal pelves were dilated. In one case there was marked dilatation of the ureters as shown by x-ray. Not all cases were examined bacteriologically. In seven, however, the pyelitis was shown to be due to the Bacillus coli.

I am convinced that it is just as much our duty to follow up these patients with pyelitis in pregnancy after they leave the hospital as it is to follow up the patients who have been treated for cancer, because a certain number of patients are proved to have a residuum of trouble in the kidneys and ureters.

In corroboration of Dr. Hofbauer's report that pituitary extract is valuable in the treatment of pyelitis, I may say that recently in one of my ureteral transplant cases there was no flow of urine from the rectum in thirty-six hours. I became quite alarmed for fear I had constricted the ureter and gave a dose of pituitrin with the result that the urine immediately appeared in the rectum.

DR. DANFORTH (closing).—I agree with Dr. Beck about importance of the catheter merely as a means of drainage. We have tried lavage of the kidney, with antiseptics and without, and are in favor of depending on the use of the catheter. We insure the permeability of the catheter by passing some salt solution through it at first and also afterward, if it becomes plugged.

Dr. Hofbauer's demonstration quite probably explains why so frequently we found obstruction at the vesical ostium of the urethra. In most of our cases we

had obstruction at that point, and we shall be glad to try out his suggestion of the use of pituitrin.

Replying to Dr. Nicholson's question we practically always leave the catheter in from 24 to 36 hours, although frequently we leave it longer than that if the patient is seriously sick. We rarely have had a resort to artificial abortion.

DR. JOHN OSBORN POLAK, Brooklyn, N. Y., presented a paper entitled **Study of the Effects of Blood Transfusions on Obstetric and Gynecologic Conditions.** (For original article see October, 1927, issue, page 537.)

DISCUSSION

DR. GEORGE GRAY WARD, NEW YORK CITY.—In October, 1924, I advocated this procedure as a prophylactic measure, after an experience at the Woman's Hospital of some two years, using it to build up the patient prior to operation rather than as a last resort measure. At the Woman's Hospital, we have used the Unger method and the Seannel apparatus. We stress the importance of bringing the gynecologic patient to operation with sufficient blood to go through the ordeal, especially as among gynecologic patients many have been subject to hemorrhages which have reduced their resistance, especially in fibroids. Also in some of the plastic cases we did not realize the extent of the oozing, and with a low red blood count, the additional 200 or 300 c.c. of blood lost is sufficient to make a very marked difference in convalescence, often prolonging it considerably.

We have also found that it is a very valuable procedure in fortifying our cancer cases. When we use radium, we make a practice of transfusing the patient if possible, and we feel that the patient is distinctly benefited by being better able to combat the toxic condition and in making a very much better recovery from the irradiation.

The average amount of blood used in these transfusions was about 500 c.c., which is easy to get. It is harder perhaps to get 1000 c.c. as that amount will more or less weaken the donor.

In giving transfusions it is necessary that the interne should be properly trained to do this because, while we may count on the laboratory to make the typing, etc., we often need this on a Sunday or holiday when the laboratory technicians are not there, so we have our interne trained to type and match the blood, requiring him to pass a practical examination by the pathologist before being allowed to do this alone.

In 1924 I reported 282 cases, 50 per cent of which were prophylactic cases. Since that time, in a second series, we reported 291 cases, of which 263 or 90 per cent were prophylactic, and 28 or 10 per cent were emergencies, making a grand total of 573 cases.

I wish to sound a word of caution as to the danger of internes doing this as a routine procedure. Accidents have occurred by our not appreciating fully the dangers that exist. We had two sudden deaths, and soon afterward two cases of collapse in private patients after only 200 c.c. of blood had been given, though these patients recovered quickly. We then began to look into the matter and found that there had been some carelessness in technic or selection of case. The danger is that the patient's heart may not stand transfusion in these depleted cases, and cardiac dilatation may occur. We believe that it is not wise to transfuse while the patient is under an anesthetic, for one cannot tell what the reaction is, and we avoid that except in emergencies.

DR. JOSEPH L. BAER, CHICAGO, ILL.—Recently a new classification for grouping has appeared, the so-called agglutinogen classification which depends upon the

fact that the patient has either no agglutinin substances, or one of two such substances, or both kinds. Then the zero group contains none and is the universal donor. The *A* group contains one. The *B* group contains another and the *A-B* contains both. Zero can give to anybody; *A* can give to *A* or *A-B*; *B* can give to *B* or *A-B*, and *A-B* can give only to *A-B*.

At the Michael Reese Hospital maternity transfusions were limited to infants for many years. The surgical department has been developing a greater frequency of blood transfusions. The hospital has a very considerable group of donors. There are fifty medical students on call all the time. Each of them is given the Wassermann test every six weeks. Each one is known in his proper classification. The checking is done immediately before the transfusion. It is much better to give a small transfusion, wait a few hours and give another small one preoperative than to give one large transfusion. If a second transfusion is given of the same group from which the first donor came, it is nevertheless necessary to check again with the second apparently identical group donor, because McQuarry and Hopkins showed in 1923 that there are subgroups, and there may be disaster unless each successive donor is checked regardless of the fact that he is in the same group.

DR. FRANK W. LYNCH, SAN FRANCISCO, CAL.—We first used blood transfusions for replacement in preparation for operation, and secondly as a stimulation for the marrow cells to increase the output. We then gave it chiefly to patients with hemorrhage, viz., fibroids, essential menorrhagia, and uterine cancers. But as we have developed transfusions and given them in pregnancy for pernicious vomiting and other toxemias and to postoperative patients who were not doing well but who had no evidence of infection, we came to appreciate that the chief value of blood was that of the most assimilable and lasting of all foods.

Our cases are not quite like those of pernicious anemia where the marrow cells are making as much blood as possible and cannot be stimulated to greater productivity. Our cases are acute conditions rather than chronic. The toxemias, postoperative cases, and cancers have their own problem, and we use the blood chiefly as food and in lesser measure to stimulate the hematopoietic cells which may not be acting to full capacity. We have come to believe also that blood given by transfusion does not aid healing nearly as much as if the patient made it herself. Thus, if we take a patient with low hemoglobin, 18 to 20 per cent, and build her up to approximately 50 per cent hemoglobin and 3,500,000 red blood cells, it does not follow that her power to withstand infection is as great as if she had developed for herself the same blood count. We have learned from experience that, when treating a gynecologic patient with less than 20 per cent hemoglobin but who needs much operative work, it is well to build her up by transfusion to at least 50 per cent hemoglobin, and then do as little surgery as seems imperative and not forget that in such cases the blood as ordinarily given has little more than food value.

For these reasons we are not insistent that the staff transfuse only whole blood except in the presence of infections. Citrated blood has its value. We are more interested in having the patient get the blood for food than in the method of transfusion.

DR. J. HOFBAUER, BALTIMORE, MD.—I desire to present a brief report of the work done in the Johns Hopkins Hospital on the subject under consideration.

The importance of blood transfusion as an early treatment in severe cases of premature separation of the normally implanted placenta was emphasized last year in our studies on histamine intoxication. In view of the great reduction of blood volume in actually effective circulation, transfusion in this condition serves the purpose of restoring the deficient blood volume. (See AMERICAN JOURNAL OF OBSTETRICS AND GENECOLOGY, vol. xii.)

With regard to the effect of blood transfusion in cases of puerperal infection, the available evidence supports the view that in all probability we have to deal here with the action of foreign protein therapy on the reticuloendothelial system. However, it is still a matter of controversy whether transfusion may actually confer on the organism a higher resistance in acute or more protracted cases of infection.

The researches of recent years have added considerably to our knowledge of the function of both the endothelium and the reticuloendothelium system as organs of defense and elaboration of antibodies, and evidence has been accumulating to show that local immunity may be essentially due to a demonstrable activity of phagocytic cells. On the basis of this evidence investigations have been carried out in the obstetric department of the Johns Hopkins Hospital to search for such therapeutic agents as would elicit evident reactions on the reticuloendothelial apparatus and by so doing would potentiate the therapeutic effect of blood transfusion. Stimulated by some advances in our knowledge of hormone activities on one hand and the effect of hypertonic solutions on the other, for purposes of studying this question, pituitary extract and hypertonic solutions of glucose were chosen. Our investigations were conducted first on normal puerperal women from the third to the fifth day of the puerperium, with a view of ascertaining, if possible, the influence of these substances on the bone marrow and the spleen.

As an invariable result in these experiments the following phenomena could be recorded: There occurred a marked increase in small lymphocytes and monocytes. Myelocytes and transitional cells made their appearance. In most cases a definite increase of platelets could be seen. The leucopenia as an immediate result of the infection was followed by a moderate leucocytosis. A considerable increase in the red blood count was observed after the administration of 25 per cent glucose.

It was an essential feature of our observations that an enhanced reaction could be seen whenever the injection of pituitrin (0.5 c.c. each dose) was combined with a subsequent infusion of 500 c.c. of 10-15 per cent glucose, or 150 c.c. of a 25 per cent solution.

The data given serve to illustrate the fact that the injection of pituitary extract in puerperal women exerts a stimulating influence on the bone marrow, as evidenced by the outpouring in the puerperal blood of both early elements and such cells as are known to increase the resistance of the organism when infected. And the considerable increase in the number of platelets points to a temporary blocking of the reticuloendothelial system by the injection of pituitrin.

The bearing of these observations on the treatment of puerperal infection is worthy of consideration, particularly when it is recalled that a comparatively small increase in the salt concentration of blood has been found to have a considerable influence on the bactericidal power of the blood.

In view of these results, the injection of pituitary extract fifteen to twenty-five minutes prior to blood transfusion is now being routinely employed in cases of puerperal infection. The results obtained seemed to warrant the conclusion that by this combination transfusion is brought to its height of functional activity and better clinical results can be secured. In due intervals hypertonic glucose solution is given intravenously (1) as a protective agent against fatty infiltration of the parenchyma, and (2) as a stimulant of phagocytic tissue elements. Our clinical observations seem to indicate that infusion of glucose should be considered particularly whenever there can be seen a tendency toward a localization of the infectious process. It is hoped that further work may be profitable in this direction.

DR. JAMES R. GOODALL, MONTREAL, CANADA.—Altogether we have transfused twenty-two cases of puerperal sepsis, and my experience has been that in only two cases was there any advantage to be derived from this procedure. In the other

twenty there were eighteen cases in which a very severe reaction occurred, so severe in five of them that the patient was practically moribund within one-half hour. In view of this we have proceeded with very great caution in the matter of transfusion in the cases of sepsis.

In the last three cases of severe puerperal sepsis which have come under my observation, every donor, professional and voluntary, proved unsatisfactory. The doctor who has to do with the grouping in the hospital and who does nothing but that told me that there was not one donor that would quite agree, and I feared to do the transfusion lest the reaction would be too severe. Those three patients all got well, and this leads to the question whether the recovery is always due to the transfusion. We all know that in severe cases of streptococcus infection recovery sometimes takes place by crisis, just as in pneumonia. In view of the fact that there were only two cases out of the twenty-two benefited, it would be hard to draw any conclusion as to the efficacy of transfusion. We have come to the point—and I think I can speak for some of my confreres—where we hesitate to transfuse in puerperal sepsis, and I believe that any advantage that may accrue from the transfusion may be attributed to action other than the resultant of the transfusion.

DR. FREDERICK J. TAUSSIG, ST. LOUIS, MO.—I should like to report briefly on the work at the Washington University Medical School, largely done by Dr. W. J. Dieckman. We have done in the past four years 227 transfusions on 106 patients, using the syringe cannula method in 10 cases and the citrate method in 217. A new citrate method, which was suggested by Dr. Dieckman, has been used in 177 cases, and the reactions as a result of this improvement in our technic have fallen from 45 per cent by the old citrate method to 14 per cent by the new citrate method. Dr. Dieckman himself has done 30 without any reaction, so I believe with the proper apparatus and technic, this new citrate method can be used without danger.

The amount of blood given has averaged 560 c.c. in volume and the largest amount of blood given was 850 c.c. The largest number of transfusions to a patient was 11.

The particular point that I wish to stress is the results in repeated transfusions at short intervals. I think the mistake we have made in the past has been to give transfusions at intervals of from five to seven days instead of watching the blood picture, the viscosity of the blood and the hemoglobin, and insisting upon giving a transfusion every second or third day until the blood picture has risen to the proper amount. If we do this, we can, according to our experience, shorten the stay of the patient in the hospital very materially.

DR. GEORGE W. KOSMAK, NEW YORK CITY.—In this discussion on the preoperative preparation of the patient I think we should bear another procedure in mind, especially in fibroid cases that are more or less advanced, in whom we find a myocarditis present. In these cases a proper preoperative digitalization of the patient should not be neglected.

DR. C. H. DAVIS, MILWAUKEE, WIS.—In some recent experimental work, at Columbia Hospital, Yates and Raine have shown that thirty minutes of gas-oxygen anesthesia without an operation will reduce the oxygen-carrying power of the blood from 10 to 20 per cent. Five hundred c.c. of whole blood after an operation will bring the oxygen-carrying power of blood back to normal. This shows that a transfusion does more than supply fluid and food. Possibly one of the chief values of whole blood transfusion is to boost the oxygen-carrying power.

Regarding the method of transfusion, we have under way at Columbia Hospital a check-up on some 500 transfusions to find out the percentage of reactions with

each method. The indications are that the paraffin tube method gives less reaction than the syringe, and much better results than are obtained with citrated blood. We believe that the citrate method should be discarded and that whenever possible the paraffin tube method used.

In some of the critical cases the bad results may be due to a foreign protein reaction. In one of our patients it was necessary to make skin tests with five donors before a suitable one could be found, although their bloods apparently matched perfectly.

DR. LILIAN K. P. FARRAR, NEW YORK CITY.—I kept a record of the first 300 blood transfusions given by the internes in the Woman's Hospital, and found the percentage of reactions that each interne had. As the laboratory was then typing and matching all blood, and the internes were using the same blood transfusion apparatus, it seemed there should not be much difference in their percentages, but I found the percentages varied from 0 per cent with a few internes to 75 and 80 per cent with two other internes. The majority of the internes had percentages of approximately 8 to 10 per cent, and the total average for all the transfusions given was 25 per cent. The reaction seemed to occur when a very fine needle had been used, so that the blood platelets were crushed, and also when the syringe used was jerked or pushed roughly if the plunger was bound.

Another point is that we do not always consider the amount of blood to be given relative to the weight of the patient or relative to the immediate need of the recipient. A patient of two hundred pounds weight is quite a different proposition from one who weighs only one hundred pounds, and a patient who has just had a severe hemorrhage can receive more blood without having a reaction than a patient who has had a secondary anemia for some time.

Dr. Ward cautioned against giving transfusions while the patient was under an anesthetic, except in an emergency. The reason for this is that a patient will often complain of a feeling of distress a minute or so before dangerous symptoms are noted by the person making the transfusion. That minute may mean the saving of the patient's life. Hypodermics, preferably of adrenalin solution, should be ready for possible severe reactions, to be given either intramuscularly or by intravenous injection or even into the heart muscle, if the patient is in collapse.

The blood transfusion apparatus that we have found most satisfactory in the Woman's Hospital is the Scannell, owing to its simplicity. It is a one-man syringe, requiring no assistant, and consequently there is less liability for error.

DR. WILLIAM R. NICHOLSON, PHILADELPHIA, PA.—I simply want to accentuate, from a bitter experience, the statement made by Dr. Ward and Dr. Farrar that no patient should receive transfusion under anesthesia. We had a case of placenta previa that I was told needed a cesarean section, and I found it needed simply a rapid version. The woman was in very good condition when I finished, but the transfusion being ready, I allowed it to be given before she was entirely out of ether, and she died within two hours.

DR. POLAK (closing).—In regard to Dr. King's question I would say that we have our senior class and the internes grouped and tested with the Wassermann test. These are checked up, and we get our donors from those sources. We feel the responsibility very definitely.

Regarding Dr. Piper's question, I want to clear up one point. The temperature in sepsis has a rise and a fall as a rule. We do not transfuse at the peak, but during the remission which occurs usually in the morning or some time during the day. The temperature goes up at night to 104° F., in the morning it is 101°. We would transfuse at 101° and not wait for it to go up again.

Whether the patient I spoke of who was in the hospital one hundred and two days would have recovered without transfusion, I do not know, but I do not believe she would.

Both of these cases show the importance of time, which is a very essential element, and food, and possibly stimulation of the marrow cells. As to the matching, I have a patient of Group 4 who was matched with 12 donors. All during her sepsis we never succeeded in getting one donor that would match with her. It was interesting that three of these donors who had been refused matched as soon as she came down to normal. This shows the importance of matching immediately before transfusion.

We feel with Dr. Taussig that transfusions should be repeated. We do not wait for the patient to become sick; when she has a rise of temperature and the temperature is not down within twenty-four hours, we repeat the transfusions every third day, giving the small amounts of 200 to 250 c.c.

I learned about three years ago from one of my surgical colleagues the effect of anesthesia on blood, and it was very typical of what Dr. Davis has called attention to, so we never transfuse during anesthesia nor until the anesthesia has worn off. We try to do our work under local anesthesia in the severe cases, such as our ectopics, in order to avoid the effect that it has on the oxygen-carrying power of the blood.

One other point: Preoperative cases where there are any infections, as for instance the pus tube case with exacerbations and reinfections, are poor surgical risks. Or in the parametrial cases it is surprising how boosting these patients along with transfusions and pituitrin has improved their general well-being.

DR. EDWARD C. LYON, JR., New York City (by invitation), presented a paper entitled **The Study of Stillbirths Occurring in 4000 Consecutive Confinements**. (For original article see October, 1927, issue, page 548.)

DISCUSSION

DR. HARVEY B. MATTHEWS, BROOKLYN, N. Y.—I should like to stress the definition of stillbirths. Most reports have included infant mortality. We should regard stillbirths as those that occur at or beyond the twenty-eight week only and should not be held responsible for the life of the child before the period of viability. In New York City one must report every abortion or miscarriage as a stillbirth, and I have always been very much opposed to such a scheme because it does not give a true index of the incidence of stillbirths.

The class of patients one is dealing with will, to some extent, determine the percentage of stillbirths. We find at the Long Island College Hospital and at the Methodist Episcopal Hospital two entirely different classes of patients; hence, we get a different stillbirth rate for each hospital. Again we get a different rate from those patients that are brought in or sent in by doctors who do not do competent prenatal work. Private patients too will have a different stillbirth rate. The prenatal clinic cases have the lowest stillbirth rate. Now as to a working classification of fetal deaths I would like to suggest the following: those that are dead on admission; those that die during labor but before delivery; and finally those that die during delivery.

The statistics from the Long Island College Hospital and Methodist Episcopal Hospital show about the same as Dr. Lyon's. In 2000 labors at the Long Island College Hospital, we had a stillbirth rate of 44 per 1000, including all classes of cases. A number of these cases came from extremely poor neighborhoods, were brought in by the ambulance or were referred by doctors and midwives. In 1000

cases from our prenatal clinic there was a rate of 24 per 1000. A former series from our clinic, tabulated by A. C. Beck, showed 18 per 1000. In 4000 consecutive labors at the Methodist Episcopal Hospital we had a stillbirth death rate of 24 per 1000. The private cases showed 26 per 1000, and the general ward cases 19 per 1000. Ward cases receiving prenatal care during the greater part of pregnancy showed 14 per 1000. Hence, it is evident that the stillbirth rate varies in proportion to the amount of prenatal care the patient receives, and the stratum of society to which she belongs.

In looking over the main causes of stillbirths in our series, they may be put down about in this order: toxemia, placenta previa, ablatio placenta, prolapsed or knotted cord or cord about the neck (an important factor in both the above series), macerated fetus with or without toxemia, probably syphilitic; syphilis; instrumental and breech delivery; intracranial hemorrhage and other cranial injuries; monsters and prematures.

DR. RUDOLPH W. HOLMES, CHICAGO, ILL.—The benefits which accrue from a rational routine supervision of the pregnant woman are no longer debatable. Prenatal care is one of the greatest prophylactic measures and has brought about a great amelioration of the incidence of morbidity and mortality of mothers and their children. It is unfortunate but true that only a few prenatal maladies may be recognized and then, largely only by reflection: syphilis and the toxemias, recognized in the mother, have their effects on the fetus definitely interpreted. By the x-ray gross developmental defects may be recognized. Twice it has been my fortune to recognize congenital heart disease before birth.

In Chicago, the Commissioner of Health, Dr. Bundesen, has issued a photostatic graph of the deaths, in hospitals, within the first two weeks of life: on a basis of 1000 live births, the deaths range in Chicago hospitals, from 18 to 147. This graph clearly shows that many women still go through pregnancy without prenatal care, and with something wrong in the attention during labor.

If we eliminate the inevitable sequences of the above conditions, syphilis, toxemias, maldevelopment, and unskillful obstetrics, we yet have a large number of fetal deaths of which we know little or nothing. Personal contact with a patient is essential in the proper interpretation of disease,—we have not that personal contact in the case of the unborn child. So we find a large proportion of fetal deaths are due to what Dr. Cragin denominated "congenital weakness" for lack of definite knowledge.

We know that fish produce an enormous number of eggs in the spawning season, a wise provision of nature, as so many of the eggs are lost directly or soon after fertilization has been accomplished. This biologic fact has its parallel in the human family; more children are produced than are needed. We see a similar parallel in the 200,000 ova in the newborn female child, few ever reaching perfection and fertilization.

DR. JOSEPH L. BAER, CHICAGO, ILL.—A comparison of statistics, of which this paper is an excellent example, is perfectly futile without a standardization. What is a stillbirth? The definition of viability is twenty-eight weeks, 1800 grams weight, 35 cm. length. The law of Illinois, the Bureau of Census at Washington, and the American Public Health Association recognize as a stillbirth a fetus that is born without movement, heartbeat or respiratory effort, and a fetus that is born with any one of those three phenomena is a live birth legally, quite regardless of viability. Therefore, if Hospital A chooses to regard viability as a criterion for its stillbirth incidence, Hospital B ignores viability, and Hospital C chooses to call a fetus a live birth at twenty weeks because it gasps once or twice and is then entitled to a death certificate, our figures are perfectly useless, and

until we can get some unanimity as to what constitutes a stillbirth we shall not be able to compare them.

DR. J. WHITRIDGE WILLIAMS, BALTIMORE, MD.—A number of years ago I collected and tabulated the deaths occurring in a series of 10,000 deliveries, which included all babies dying during the first two weeks of the puerperium. A considerable part of that series was before satisfactory prenatal care was employed. It was shown that the predominant cause of fetal death was syphilis, which was responsible for over 30 per cent of the deaths. The mortality of the last three years in about 3,500 cases, from the period of viability up to and including the first two weeks of the puerperium, was 6 per cent. I was very much interested in two things: first, to see that the prenatal care had reduced the deaths from syphilis from over 30 per cent to about 6 per cent. In this series, practically all the deaths from syphilis occurred in the children of women who had not had prenatal care. Consequently, intensive prenatal care has served to reduce the incidence of death from syphilis almost to the vanishing point.

The second thing that interested me in this study was to determine what proportion of the children died from cerebral injuries. Practically all of the 210 children in the series came to autopsy, and cerebral injuries were found in 6 per cent, only half the number in Dr. Lyon's report. I had expected to find it much higher. Likewise, just as he did, we found a very large incidence due to placenta previa and separation of the placenta.

The general result of my experience is that by efficient prenatal care we are able to do away almost entirely with the deaths due to syphilis. We are scarcely able to affect those due to placenta previa or premature separation. We can to some extent diminish the deaths due to toxemia. But we have a very considerable field for the reduction in the number of deaths due to dystocia, especially when associated with moderate degrees of pelvic contraction, and it is in this field that we can look forward to improvement in the future.

DR. J. P. GREENHILL, CHICAGO, ILL.—Our experience at the Chicago Lying-In Hospital has been essentially in accord with what Dr. Lyon has said concerning his study at the Woman's Hospital. However, our incidence of cerebral hemorrhage was only 19.7 per cent. We found that syphilis as a cause of stillbirth is not very significant, since it accounted for only 2.6 per cent of all our fetal deaths. The toxemias of pregnancy caused the death of a large number of fetuses, most of which were expelled prematurely. In a few of our cases pituitrin was the cause of death. The house staff practically never uses pituitrin during the first or second stage of labor, and the fetal deaths which followed the use of pituitrin occurred at the hands of attending physicians. At autopsy, babies presumably killed by the action of pituitrin showed a most intense congestion and pinpoint hemorrhages of the brain.

You may be interested to know that at the Chicago Lying-In Hospital during the past seven years we had nineteen fetuses which were monsters or had gross deformaties. Seven of this number, or 36.8 per cent were associated with placenta previa. I mention this in particular, because a few years ago I tried to emphasize the not infrequent association of fetal monstrosities and deformities with placenta previa.

DR. LYON (closing).—In regard to the fetal heart our custom now is to have the heart rate taken during the interval between contractions, and if there is an increase or decrease of 20 points, it is reported to the resident.

It is not our custom to permit pituitrin either to induce labor or to hasten the second stage, without an order from one of the attending surgeons.

DR. JOHN A. SAMPSON, Albany, N. Y., read a paper on **Peritoneal Endometriosis, Due to the Menstrual Dissemination of Endometrial Tissue into the Peritoneal Cavity.** (For original article see October, 1927, issue, page 422.)

DR. EMIL NOVAK, Baltimore, Md., read a paper entitled **Ovarian Metastasis With Cancer of the Uterine Body. Is Transtubal Implantation an Important Factor?** (For original article see October, 1927, issue, page 470.)

DISCUSSION

DR. CHARLES C. NORRIS, PHILADELPHIA, PA.—At our meeting in 1921, Sampson presented his first paper upon this subject. I believe this and his subsequent work to have been the best research along gynecologic lines for many years. As is natural with any work which has attained international interest, Sampson's conclusions have not escaped criticism. The fact that such lesions as Sampson has described occur, and occur frequently, is now recognized. Whether the Sampson cysts be the result of transtubal dissemination of desquamated menstrual endometrium or due to a metaplasia of endothelium is of secondary importance, but is the point about which most of the discussion has developed. Novak, in this country, and R. Myer, in Germany, have headed the opposition to the transtubal theory.

The chief arguments against the transtubal theory are: (a) that the intramural portion of the tubal lumen is too small to permit the passage of desquamated epithelial cells, and (b) that the desquamated endometrium is devitalized or dead. On the other hand, the arguments in favor of the transtubal theory are: (a) the location of the implants; (b) the patency of the tubes; (c) the morphology of the lesions; (d) the result of animal experiments; (e) the fact that it is usually found in association with uteri in which some obstruction to the free outflow of the menstrual blood is present, and (f) that the endometrial-like tissue in the implants undergoes changes similar to those of the corporial endometrium and does so at the same time. This latter is one of the strongest arguments in favor of the müllerian origin of the transplants.

Endometriosis is in many respects similar to peritoneal carcinomatosis, both are spread by direct seeding and by lymphatic extension. In carcinomatosis the lesion consists of embryonal, rapidly growing cells, whereas endometriosis is the result of a normal adult cell transposed to a new environment and is probably of extremely slow development. Pseudomyoma of the peritoneum also in many respects resembles both of these conditions and lies midway between the two in point of rapidity of development.

Sampson has drawn our attention to a new gynecologic disease which in advanced cases often presents a fairly typical clinical picture and may ultimately prove the solution of many formerly unexplained gynecologic lesions and possibly the source of origin of various neoplasms.

Regarding the advisability of diagnostic curettage in cases of suspected fundal carcinoma, I believe the operation has a definite field. Fundal carcinoma is a malignant form of cancer. In an analysis of over 100 cases of this condition from the gynecologic clinic of the hospital of the University of Pennsylvania, the three year salvage was only about 34 per cent. Early diagnosis is essential; in our early cases we saved about 60 per cent to 70 per cent. The manifestations during the early stage are often vague and the earlier the disease, the less prominent are the symptoms. Bleeding and discharge are the chief symptoms. In patients in whom the disease develops at about the time of the menopause, the clinical diagnosis

is often especially difficult. Curettage offers a practically positive means of arriving at a diagnosis. The Clark test which consists in gently raking over the surface of the endometrial cavity with the point of a uterine sound is of distinct value, in that carcinoma of the fundus is a friable, vascular growth, and hence, this test is followed by a slight trickle of blood. This test should be performed under strict asepsis and can be utilized in the office. It is not positive, but if blood follows the sound, curettage should certainly be performed.

Accepting as I do the Sampson theory of transtubal dissemination of normal endometrium, it is but natural to feel that diagnostic curettage may occasionally result in the transtubal dissemination of fundal carcinoma. That this does not often occur is shown by the fact that actually better results were secured in our series of fundal carcinoma in those cases in which diagnostic curettage was performed than in those which were not submitted to this procedure. The explanation of this is probably that the cases upon whom diagnostic curettage was required were the earlier ones. I do not believe curettage should be performed as a routine or lightly undertaken. There are, however, a good many cases in which it offers the only method of arriving at a positive diagnosis, short of hysterectomy. Were we to eliminate diagnostic curettage from the list of justifiable operations, it would mean either that many benign uteri would be sacrificed or that many early carcinoma would be permitted to develop to the advanced stage. Diagnostic curettage can be safeguarded by thorough dilatation of the cervix, the avoidance of irrigation of the uterine cavity following the operation, or the avoidance of uterine packing, or anything which may interfere with the free drainage of the cavity. The application of radium at the completion of the operation is a definite and further safeguard. If the patient is merely suffering from a myopathic hemorrhage, the radium will nearly certainly cure the condition, whereas if a carcinoma has been curetted, the action of the radium is distinctly beneficial and probably destroys any loose cells which may have been left in the uterine cavity. As these suspicious cases generally occur in elderly women, the application of the radium has no drawbacks. I do not employ frozen sections for the examination of material obtained by curettage. The diagnosis, especially in the early cases, is such an important one that I prefer to delay a few hours and thus secure better specimens.

I would like to place on record the history of a case which I believe to have been one of transtubal dissemination of a fundal carcinoma. A woman, twenty-eight years of age, was brought to our ward with a diagnosis of incomplete abortion. The usual palliative treatment failed to check the hemorrhage. A curettage was performed and the specimens obtained were examined according to the routine method. The specimens were found to consist chiefly of normal endometrium, but a few fragments showed undoubted adenocarcinoma. The patient had left the ward three days after the operation and moved to another city; as a result six weeks elapsed before she could be brought back and a hysterectomy performed. A carcinoma about 1 cm. in diameter was present in the fundus, both tubes were normal, a papillary carcinoma about 2 by 4 mm. was present upon the upper and outer surface of the right ovary. This tumor was identical in its histologic structure with the carcinoma in the endometrial cavity. Radium was not used in this case, and it is probable that the curettage broke up and left behind in the uterine cavity small particles of the neoplasm and that the uterine spasm which followed, forced out some of these cells through the tubes, and that some of them found lodgement upon the surface of the ovary. This case is also of interest on account of the youth of the patient. In older patients, the tubes may be atrophied and their lumen lessened in diameter and as a result transtubal dissemination is less likely. In a definite proportion of our cases in which associated ovarian and fundal carcinomas have been present, the growths have been similar in their histologic structure. I would summarize by saying that curettage should never be performed unnecessarily,

that there is a danger of transtubal dissemination in the case of a fundal carcinoma, but that this danger can be largely eliminated by attention to technic and that by not performing diagnostic curettage in suspicious cases, the patient is submitted to a far greater hazard.

DR. JOSEPH BRETTAUER, NEW YORK CITY.—I consider Dr. Sampson's point of view somewhat radical and feel inclined to endorse the principles laid down by Dr. Norris. A recent case in my experience is unique. About six months ago a young professional woman was brought to me by her doctor, to be operated upon for multiple fibroids. Excessive menorrhagia and pain were the symptoms complained of for some months prior to my first examination. The attending physician had made a rectal examination(the hymen being intact) and found multiple fibroids reaching up to the umbilicus, with a large pedunculated nodule in the right inguinal fossa. The growth increased rapidly in size, bleeding was not controlled by internal medication, and operation was strictly indicated.

A supravaginal amputation of the uterus and a left salpingo-oophorectomy were done; the left ovary contained a large Sampson cyst and was densely adherent; the right ovary apparently was normal and was left in situ. An inflammation was found in the Douglas pouch, which rectal examination proved to be an infiltrated, ulcerated condition in the lateral rectal mucosa. The upper third of the rectum was resected, and a sigmoidorectal anastomosis was made. Recovery was uneventful.

It was only through the pathologist's report that the condition, which we thought was carcinomatous, was found to be an endometrial infiltration.

I would like to know if Dr. Sampson is prepared to say that this is a malignant condition, or whether such tissue should be left after the removal of the uterus and adnexa.

DR. WILLIAM P. HEALY, NEW YORK CITY.—It seemed to me that Dr. Sampson had in a very simple way explained a condition which I had met with clinically a great many times and had been unable to explain satisfactorily. I have met with a great many instances of endometriosis occurring in the culdesac, in young women, in which the rectum was pulled up on to the posterior surface of the uterus. In the first two cases I did a major operation, removing the rectum as well as the uterus and adnexa, and received a report that did not verify a malignant lesion. Thereafter when I met with the condition, I left it intact if it were in the culdesac, and in two instances in which there were chocolate cysts in the ovaries I resected enough of each ovary, as these women were young, to leave a fair amount of normal tissue. Each of the women has since conceived twice, gone through a normal labor, and the lesion in the culdesac is still there. So there are four children in those two instances of conservative surgery.

On the other hand, I have seen some patients who have had a good deal of distress from the lesion in the culdesac. They had consulted competent surgeons; exploratory celiotomy had been done; the surgeon concluded that the lesion was inoperable and sent the patient to me for treatment with radium on the theory that a carcinoma was present. I have identified the lesion as an endometriosis and treated it, with relief of the patient's pain, and I think there is no reason to hesitate to do that and avoid surgery where the lesion is located at that point.

Dr. Sampson emphasizes the constant location of the earlier lesion on the lateral surface of the ovary where fragments of tissue may very easily become attached to the ovary and the broad ligaments, or to the ovary and the uterus, because invariably that is where we find these lesions. The ovary is always adherent and has to be separated in order to perform any operation upon it.

With regard to Dr. Novak's communication I am absolutely in accord with all he says about the importance of the lymphatic route of extension in the uterus. On the other hand, we do see frequently at the Memorial Hospital, from the stand-

point of implantation, superficial metastases along the vaginal walls in cases of adenocarcinoma of the corpus. These are not lymphatic extensions; they can be easily rubbed off; they are multiple implants and the diagnosis of adenocarcinoma of the corpus can be made from them. We do see cancer emboli in the veins of the corporeal musculature. We operate on the theory of lymphatic extension and clamp the broad ligaments widely apart immediately on opening the abdomen and do not place any instrument in the corpus until we have thoroughly clamped the broad ligaments.

As to the danger of diagnostic curettage, I agree with Dr. Novak that it should be done, but I think the major operation should be done as promptly as possible after the curettage. On the other hand, one can make a diagnosis without curetting, by removing tissue by suction with a pipette which a pathologist should recognize as carcinoma if it be present. That has been done at the suggestion of Dr. James Ewing, who felt that curettage was dangerous. This is not a difficult thing to do; however, I prefer removal by the curette.

Regarding the age of the patient, we have had at the Memorial Hospital only a few patients in the menstruating age who have had undoubted carcinoma of the corporeal endometrium. Practically every one of our patients was beyond the menstrual life. I think that is important to bear in mind from the standpoint of diagnosis and treatment.

As to the use of radium in the body of the uterus, I think it should be used only when operation cannot be done, or when one is awaiting a microscopic report of the tissue obtained.

DR. I. C. RUBIN, NEW YORK CITY.—Among the points of interest is that the tube is so narrow as not to permit the passage of endometrial fragments. During normal pregnancy within the early days of impregnation which occurs in the tube, the ovum passes into the uterine cavity, and by that time it is an appreciable structure. At this blastula stage it would be equal to the size of some of the small endometrial fragments that Dr. Sampson has found in the tube and on the surface of the peritoneum, so that narrowness of the lumen cannot be advanced as a decisive reason against the transtubal spread of endometrial fragments during menstruation,—not even the narrowest lumen in the specimen encountered by Dr. Sampson which he has shown us on the screen. It is well known that the tube lumen is capable of dilating and contracting, as in the case of the transportation of the hen's egg from ovary through oviduct to the cloaca. Furthermore, the fallopian tube is capable of peristalsis and antiperistalsis.

Secondly, it is very probable that although the desiccated part of the endometrium is dead, small fragments near the basal layer of the endometrium coming away with it and going through the tubes retain enough vitality to regenerate themselves wherever they are implanted, in the same way as the residual basal portion of the endometrium in the uterine cavity.

The third point was the presence of some stimulus during menstruation which activates the endothelium to a degree of metaplasia, sufficient to resemble endometrial structures. I believe that some time during ovulation the follicular fluid is poured out from the ovary, is taken up by the tubes and stimulates their peristalsis. It is possible that that fluid also contains a hormone which induces the endometrial reaction in the uterus itself and at the same time perhaps the decidual reactions that we are all familiar with in studying sections of the peritoneal covering of the pelvic organs removed during menses and gravidity.

As to the mechanism of transtubal migration, it is easy to conceive how the fragments can be transported along the tubal lumen into the peritoneal cavity and fall into the fimbriated gutter, which Dr. Sampson has shown us, by direct transmigration of endometrial fragments. In those cases of so-called dysmenorrhea of

the colicky type, with either a spasmodic closure of the internal os or perhaps a rigid organic stricture of the cervix, where the menstrual fluid containing its endometrial portions collects, repeated uterine spasm can easily force this menstrual blood with its endometrial fragments through the tubes. The fact also should be taken into account that if one examines a patient during menses, the uterus may be squeezed to such an extent as to force some of the menstrual fluid through the tubes, thus causing a spread of these fragments in that way.

About the relationship between curettage and the transportation of endometrial fragments with the menstrual fluid, I believe that with a large curette blocking the cervical canal while the uterus is contracting, the spasm being incited by the instrument, one can force endometrial fragments through the tubes. Secondly, so far as the transplantation of carcinoma from the uterus along the tubes is concerned, Ewing for example, believes very strongly that carcinoma is spread by curettage. To overcome the possibility of spreading cancer cells by curettage, it might be well to get a biopsy by means of a cystoscope punch and take out a fragment of any portion of the uterine cavity desired. In that way one does not cause as much trauma as with the curette. I have used this instrument for several years for the purpose of obtaining small particles of uterine mucosa in the study of the functional condition of the endometrium in cases of sterility.

DR. EMIL NOVAK, BALTIMORE, MD.—The problem of the etiology of endometriosis is a difficult one to attack directly, and the various views which have been advanced are based practically altogether upon circumstantial evidence. Dr. Sampson, in the defense of his menstrual regurgitation theory, is thus placed somewhat at a disadvantage, as experimental or clinical proof of its correctness is impossible at present. A direct method of approaching the problem would be by growing in the peritoneal cavity the endometrium cast off at menstruation, but this would be foreordained to failure, if the results of tissue culture in general are to be accepted. In the discussion of this subject before this Society last year, I suggested that tissue culture studies of the endometrium might yield important results. For some months Dr. Herbert Traut, of the gynecologic department of the Hopkins Medical School, has been carrying on such studies. He has been able to obtain ready growth of the postmenstrual, interval, and premenstrual endometrium, but has not, as yet, succeeded in getting any definite results with menstruating endometrium. This work, however, is as yet in its infancy. The work of Jacobson, who studied the transplantation of endometrium to the peritoneum of lower animals, is of interest, but throws no light on the etiology of endometriosis.

I do not know the cause of pelvic endometriosis, but I do not believe that Dr. Sampson's explanation is the correct one. As I presented the arguments against it before the Society in my paper of last year, I shall not repeat them here. I believe, for reasons which I discussed in that paper, that the explanation of the condition revolves about the fact that all the surface tissues in which ectopic endometrium may be found have the same embryonic derivation as does the endometrium,—the germinal epithelium, the pelvic peritoneum, etc. All arise from the celomic epithelium, representing merely different degrees of differentiation. What the activating cause of the differentiation into endometrium is, I do not know, but it seems quite possible that it is something derived from the tubes, which, I agree with Sampson, are commonly open. Some of the epithelial cells of the tube are apparently of definitely secretory type, and may play a part in this process, but this is only conjectural at present.

The celomic differentiation theory of endometriosis will explain certain cases which cannot be explained by the regurgitation theory, such as the endometrial islands occasionally seen at the umbilicus, in the groin, or even in the vulva.

DR. ARTHUR H. CURTIS, CHICAGO, ILL.—Dr. Healy's statement relative to the infrequency of carcinoma of the corpus uteri during the menstrual age comes as a considerable surprise to me. In my private practice alone, within the last year, I have had four of these cases. I would like to hear a few words regarding the experience of others in this respect.

In contrast with Dr. Norris, Dr. Novak, and Dr. Healy, I am definitely opposed to diagnostic curettage unless it is absolutely necessary. I venture that it is performed at least ten times as frequently as it should be. We must not forget that practically every woman who is past the menopause, ruling out easily demonstrable uterine polyps, has in the bleeding alone pathognomonic evidence of carcinoma of the uterus. In my experience only three patients have been exceptions to this rule. Two were diagnosed as having recurrence of menstruation; one, four years after supposed menopause, the other, five years after supposed menopause, because they had breast discomfort and other phenomena suggestive of oncoming menses before the bleeding occurred.

DR. NORRIS—I did not infer in my discussion that I thought diagnostic curettage should be used routinely in all cases. I meant to convey the idea that diagnostic curettage has a definite place in doubtful cases and that I believe many cases could only be diagnosed in that way, particularly the early ones.

DR. SAMPSON (closing).—I have encountered only six cases of ovarian carcinoma associated with a similar growth, apparently arising in the uterine mucosa. Three of these were reported in the paper referred to by Dr. Novak. I have been greatly interested in the study of the lymphatics of the uterus as channels for the dissemination of cancer from that organ. The lymphatic distribution of cancer from the uterus to the ovary was not considered in this article, because I was not quite sure that it could occur, and even so I did not think that it applied in these three cases.

In one patient both an adenocarcinoma and possibly a stromal celled sarcoma of the uterine mucosa were present. There was an associated peritoneal carcinomatosis or sarcomatosis (Fig. 30 of previous article), in which the lesions were all superficial. These were present on the surfaces of both ovaries and also on the terminal loop of the ileum as well as on other structures in the pelvis. It seemed to me that the patent tubes offered the best explanation for the distribution of the peritoneal implantations as well as those on the surfaces of the ovaries. In another patient, a peritoneal carcinosis, with a distribution readily attributed to material escaping through the patent tubes (Fig. 38) was associated with a carcinoma of the uterine mucosa. A small implantation-like lesion of cancer was present on the surface of one of the ovaries. In the third case (Fig. 46), a papillary type of adenocarcinoma was present in both ovaries and apparently had developed on the surface of these organs. There was an associated adenocarcinoma of the uterine mucosa evidently arising from the uterine epithelium. Both tubes were patent.

Since this article was published, I have had three additional cases of carcinoma of the ovary associated with a similar growth, apparently arising in the uterine mucosa. In one the growth in the ovary and in the uterus was extensive and that in the uterus apparently arose from the uterine epithelium. There was no evidence of cancer on the surface of the ovary. It would seem that if one was secondary to the other, the cancer must have been transmitted through vascular channels, and I would favor the veins rather than the lymphatics. I have never been able satisfactorily to inject the lymphatics in a retrograde manner. The intrinsic veins of both the uterus and ovary are easily injected through the uterine and ovarian veins. Fragments of cancer were found in the lumen of the interstitial portion of the tube. It was a difficult operation, and in handling the uterus, bits of cancer in the uterine cavity might easily have been forced into the lumen of the tube.

In the second case of this series an adenocarcinoma was present in one cornu of a double uterus (single cervix). The fimbriated end of the tube of that side was occluded and fused with the surface of the ovary. Multiple patches of cancer had arisen in the mucosa of the distal portion of the tube and fragments of cancer were found in its lumen. Cancer was present on the surface of the ovary adherent to the tube and also enmeshed in the surrounding adhesions. I believe that fragments of cancer escaped from the uterine cavity through the tube and became implanted on the surface of the ovary and that subsequently the fimbriated end of the tube became occluded as it does in the reaction to bacterial infection.

The third case was even more interesting. The patient, aged fifty, married and never pregnant, was menstruating regularly, she thought, after a temporary cessation of her menses. On examination an indurated mass was palpated in the posterior culdesac which presented in the vaginal vault behind the cervix. A preoperative diagnosis of endometriosis was made. At operation, implantation-like lesions were found on the lateral surface of both ovaries, appearing exactly like the lesions of a benign endometriosis. The bottom of the posterior culdesac was occluded by the fusion of the rectum with the cervix, as occurs in a benign endometriosis in this situation. Both tubes and ovaries, the uterus, the mass in the culdesac, together with a portion of the posterior vaginal wall, were removed. On incising the uterus, an evident cancer of its mucosa was present. Even then I thought it was associated with a benign endometriosis of the ovaries and in the culdesac. To my surprise the implantation-like lesions on the surface of the ovaries and in the culdesac had the same histologic structure as that of the cancer of the uterus. Many theories may be advanced to explain the distribution of the cancer in this case. I believe that the implantation of fragments of cancer escaping from the uterine cavity through the patent tubes is the most logical theory. I wish that I might have had the opportunity to study more cases of cancer of the body of the uterus associated with a similar growth in the ovary. In four of the six cases which I have studied, the patent tubes offered to me the most logical avenue, by which the cancer was carried from the uterus to the ovary.

Dr. Novak has referred to my practice of ligating the fimbriated ends of the tubes, to prevent the dissemination of cancer into the field of operation, before handling the uterus in abdominal hysterectomy, when cancer of the body of the uterus is suspected or known to be present. It is quickly done, and I believe that it increases the chance of a permament cure. I have found fragments of cancer in the tubes of five uteri removed for cancer of the body of that organ. There had been a preliminary diagnostic curettage in four of these.

I still follow the rules laid down in my previous article to prevent the dissemination of cancer in the diagnosis and treatment of cancer of the body of the uterus. They are as follows:

1. A patient in whom cancer of the body of the uterus is suspected should be examined with great care and gentleness.

2. The diagnostic curettage should be employed only in doubtful cases or poor operative risks and, if used, should be done very gently.

3. Radium should not be used, as the insertion of the capsule containing the radium acts as a plunger of a piston syringe, forcing contents of the uterine cavity into the tubes.

4. Abdominal hysterectomy with the least possible manipulation of the uterus and the closure of the channels, through which material may escape from the uterus into the field of operation, offer the best chance for a permanent cure. The fimbriated ends of the fallopian tubes should be first ligated; the ovarian vessels, round ligaments, and uterine vessels should be doubly ligated, cutting between

the ligatures; the vagina should be clamped below the cervix and carefully cleansed before severing the vagina below the clamp and removing the uterus.

I have been criticized for my practice of using "the diagnostic curettage in patients with uterine bleeding only in those in whom I do not suspect cancer or when I considered the patient a poor operative risk." If the patient is past the menopause and the bleeding is obviously coming from the body of the uterus and is increased by bimanual palpation, I suspect a cancer of the body of the uterus. In younger women and, especially in patients suggesting a myofibrosis, I do not suspect cancer and a diagnostic curettage is done. Occasionally carcinoma is found in the scrapings obtained by curettage from these patients and occasionally, but very rarely, a uterus is removed when cancer was suspected and it is not found.

This month a patient came under my care with a history of uterine bleeding of several months duration. The uterus was irregularly enlarged, and a diagnosis of multiple leiomyomas was made. I thought that a carcinoma of the body of the uterus was also present. The patient was large, anemic, seventy-two years of age, and appeared to be a poor operative risk. For these reasons a diagnostic curettage was done and adenocarcinoma was found. I hesitated between the use of radium and the removal of the uterus, but finally decided on the latter. A few days later the uterus was removed. At operation the posterior surface of the uterus and other structures in the culdesac were stained with blood, and the left tube was filled with blood. The uterus contained multiple leiomyomas. It was evident that the chance for a permament cure had been greatly lessened by the curettage.

Dr. Scott asked about the origin of the stroma in misplaced endometrial tissue, whether uterine epithelium transplanted to other parts of the body carries stroma with it or may develop it from the tissue in which it lodges. The same question may be asked of the stroma surrounding the uterine epithelium of an endometriosis arising from the invasion of the uterine wall by the mucosa lining the uterine cavity. In both instances it sometimes is difficult to determine whether the stroma is arising from or replacing the tissues invaded. I have thought that in both situations stroma, at times, might arise from the tissues of its host.

Dr. Brettauer asked about the treatment of endometriosis of the sigmoid and whether or not it was malignant. Cancer invades, metastasizes by implantation and through vascular channels. Furthermore, it is lawless and continues to grow, unless it is entirely removed or destroyed. Endometrial tissue sometimes is invasive, and I believe may metastasize by implantation and through vascular channels. Fortunately it is not lawless but it subservient to the function of the ovary. Dr. William P. Graves has brought out an excellent point in the treatment of extensive endometriosis of the sigmoid with resulting narrowing of the lumen of the intestine, and that is not to resect the sigmoid but to remove all ovarian tissue and make a temporary colostomy. I have tried this in one case with excellent results.

I wish I knew more about the so-called implantations of cancer sometimes found in the vaginal wall of patients with cancer of the body of the uterus. I have thought that some of these were implantations and others might be metastases, and I would favor the veins rather than the lymphatics, as metastases of chorioepithelioma occur in this situation.

I believe that the ovaries and the tubes are the chief distributing agents for the cause of peritoneal endometriosis. Patent tubes evidently play an important rôle in the etiology of this condition. The endometrial tissue in the peritoneal lesions resulting from the escape of material from the ovaries and tubes must arise either from the implantation of cells carried with it or from a metaplasia of the peritoneal mesothelium brought about by its stimulation by some specific irritant present in this material.

Judging by the short time required for blood to escape from the uterine cavity

into the tubes during curettage, menstrual blood which often contains bits of the uterine mucosa might likewise quickly pass from the uterine cavity into the tubes.

Cron and Gey have recently shown, by tissue culture, that the endometrium cast off by menstruation is viable. (AM. JOUR. OBST. AND GYNEC., 1927, xiii, No. 5, pp. 645-647.)

Replying to Dr. Curtis' question whether I favor diagnostic curettage in women who have inexplainable uterine bleeding prior to the menopause: In most cases I do, unless I find some other reason for removing the uterus. If the patient is past the menopause and has uterine bleeding, I suspect cancer; if before menopause, I do not suspect it. Every patient with uterine bleeding that comes under my care is advised to have either a curettage or an hysterectomy, which depends on the individual case.

DR. CARL HENRY DAVIS, MILWAUKEE, WIS.—The difficulty in the tissue culture work referred to by Dr. Sampson is in being absolutely sure that one is getting tissue that is being cast off. Tissue removed by a dull curette, does not answer strict requirements. It is also possible that a pipette may dislodge tissue that had not already been cast off. Endometrial tissue obtained from vaginal secretions frequently shows deeply staining nuclei and is believed to be alive, but it cannot be used for cultural purposes because of bacteria. Mr. Gey has grown with ease bits of tissue obtained from the interior of a uterus which I removed from the patient during menstruation.

DR. NOVAK (closing).—As most women with adenocarcinoma of the uterus are well beyond middle life, the tubes are small and atrophic, with probably no peristaltic activity, so that it would be hard to conceive that they could transmit cancer material outward to the peritoneum. On the other hand, I was surprised to hear that Dr. Healey had encountered only two cases in women still in the menstruating age. In almost all the reports in the literature, the experience appears to have been that nearly one-fourth of the cases occur in women not over fifty. Our own study showed about the same incidence. The diagnostic method mentioned by Dr. Healey, of aspirating material from the uterus by a pipette, can scarcely be of value except in the advanced case. It would be very unreliable, it seems to me, in the cases of early or circumscribed type, especially if the growth be high up in the uterine cavity, for in these it could hardly be expected that any material could be sucked out with a pipette.

In the additional case reported today by Dr. Sampson, in which the distribution of the cancer in the pelvis resembled that of endometriosis, it seems to me, as Dr. Sampson anticipated, that the route was probably lymphatic. I had rather expected that Dr. Sampson might have suggested that there had been a malignant degeneration in an originally benign endometriosis, as he has reported several analagous cases in the ovary.

I feel rather strongly about the importance of diagnostic curettage in all except the rather obvious cases of adenocarcinoma. Regardless of what we suspect clinically, we are sure to meet many surprises. At times we will find cancer where we did not suspect it, at other times we will be agreeably surprised to find no cancer where we were almost sure of its existence. It is therefore, to my mind, not justifiable, except in the occasional case, to be guided as to the advisability of panhysterectomy by clinical impressions, when we have at our disposal, in diagnostic curettage, a quick and certain means of settling the question. This should be urged more, rather than less, widely, for there is no question that too many uteri have been removed unnecessarily because of clinical suspicion alone. Even in older women, uterine bleeding does not invariably mean cancer. On the other hand, bleeding in women below the menopausal age may, in a not inconsiderable proportion,

be due to cancer. I know of no other way of determining this point except by diagnostic curettage, preferably, as I stated in my paper, associated with immediate diagnosis from a frozen section, and followed at once, if cancer be found, by radical operation. In no other way can we be reasonably sure of not subjecting a certain number of women unnecessarily to a grave operation, and in no other way can we save another large group by recognizing and eradicating cancer in an early, easily curable stage. If a relative of mine beyond fifty had uterine bleeding, which was not profuse or of very long duration, or if such a relative below fifty had uterine bleeding, of any amount or duration; if, in other words, we were not dealing with a case of very obvious cancer, I should not want even an expert operator to perform a panhysterectomy until the presence of cancer had been demonstrated by diagnostic curettage.

DR. EDWARD A. SCHUMANN, Philadelphia, Pa., presented a paper entitled **Observations Upon the Coexistence of Carcinoma Fundus Uteri and Pregnancy.** (For original article see October, 1927, issue, page 573.)

DR. JAMES C. MASSON, Rochester, Minn., read a paper on **Total Versus Subtotal Abdominal Hysterectomy.** (For original article see October, 1927, issue, page 486.)

DISCUSSION

DR. FRANK A. PEMBERTON, BOSTON, MASS. (by invitation).—I will discuss Dr. Masson's paper. I am much surprised to find that I have no figures that compare with his at all. At the Free Hospital for Women, in Boston, from 1894 to 1926, there have been done 2,066 supravaginal hysterectomies for nonmalignant conditions, and in the same time only 22 complete hysterectomies for nonmalignant conditions. Supravaginal hysterectomy was done for fibroids in 995 cases, for pelvic inflammation in 762, and the rest were for various diseases. The reason for using the supravaginal method is that we believe there is somewhat less mortality and morbidity. We think the operation is easier, that there is less danger of sepsis, and that the vagina is not shortened at all. We believe that it is shortened if the cervix is removed. To prevent future trouble from leaving the cervix in, we examine it carefully after the patient is anesthetized, do a biopsy if necessary, repair lacerations, cauterize it if endocervicitis is present, or amputate it if it is hypertrophied. We do any other plastic work that may be necessary and then the supravaginal hysterectomy. We have had no sepsis from cauterizing the cervix.

In regard to coring out the cervix, we have done that only six times. We amputate below the internal os by a wedge-shaped incision and leave very little of the mucosa of the cervix. We find there is danger, in coring out the cervix, of a postoperative hemorrhage, either immediately after or from eight to ten days later.

We always do a myomectomy if possible, and we feel that there are less chances of getting adhesions by doing a suspension also.

We have seen 19 cases of carcinoma of the cervix after supravaginal hysterectomy. Of those 19 cases careful examination and study of the history showed that 10 of them had no cancer at the time of the hysterectomy; 5 did have cancer, and in 4 there was a question as to whether they had or not. Ten of these 19 cases had been operated upon at the Free Hospital, and 2 of them probably had cancer at the time of the hysterectomy.

DR. JOHN O. POLAK, BROOKLYN, N. Y.—The important point in these papers, it seems to me, is the question of the incidence of cancer in the stump after supra-

vaginal hysterectomy. While I am thoroughly in accord with the speaker that probably the average operator can do a supravaginal hysterectomy with greater facility than a panhysterectomy, I believe that if he is going to do a supravaginal hysterectomy, he must take into consideration the fact that cancer may occur in the retained stump, that it is a definite entity, and that this structure must be taken care of not only because of the fact of the cancer, but because of the incidence of cervicitis which is so frequently caused by trauma. Whether this is taken care of by an excision of the cervix or with the cautery, which we are using at the present time, or whether it is done by panhysterectomy is immaterial.

DR. WILLIAM P. HEALY, NEW YORK CITY.—There is no doubt that Dr. Schumann's case is an unique instance of carcinoma in the corporeal endometrium, and I think it is very fortunate that it is unique, because otherwise what an unsatisfactory situation there would be in the presence of bleeding of any type in an early pregnancy. Instead of putting the patient to bed and trying to prevent an early abortion, it would be necessary to empty the uterus.

I have stated that carcinoma of the corporeal endometrium practically never occurs during the childbearing period of life. I had a patient very recently, only thirty-seven years of age, who had carcinoma of the corporeal endometrium, but she had already entered her menopause; she had not menstruated for two years. Almost every patient I have seen had stopped menstruating. I do not mention any age, but they have invariably had an amenorrhea over several months indicating that they were entering the normal menopause.

THE OBSTETRICAL SOCIETY OF PHILADELPHIA

STATED MEETING, FEBRUARY 3, 1927

DR. JAMES F. CARRELL, of Philadelphia, described **A Case of Secondary Abdominal Pregnancy.**

Mrs. C. G., aged forty, was first seen on October 2, 1926. Her only acute illness was a mild attack of scarlet fever in early childhood. Until three years ago menstruation was regular every twenty-eight days, but since 1923 it usually came on every three weeks. The discharge was quite free and was occasionally accompanied by clots. The last period occurred on June 15, 1926, was of five days' duration, associated with the expulsion of several clots and accompanied by considerable pain. This period was followed by a brownish, vaginal discharge.

The patient was married at the age of twenty and had had four previous pregnancies. Three went to full term, and labor took place normally. One pregnancy terminated in a miscarriage at four and one-half months, shortly after the birth of the first child. She was widowed and remarried nine years ago, and had not been pregnant since the second marriage.

In the early part of July she was examined, and a diagnosis of uterine myoma was made. Accordingly, she was advised to have a series of roentgen-ray treatments and was exposed on several occasions to cross-fire.

On July 24 she was seized with a very severe attack of abdominal pain immediately after an x-ray exposure. Each subsequent x-ray treatment precipitated a similar attack of pain. There was no nausea or vomiting.

Examination on October 2 showed the abdomen slightly distended and moderately rigid, and the entire lower portion was exquisitely tender. A large, painful, and

tender mass was found rising out of the pelvis, rather rotund in outline, which seemed to be fairly adherent in the left iliac fossa. There was no vaginal discharge, and the breasts were negative.

Digital examination disclosed the cervix high up in the vaginal vault, displaced far to the left, reached with difficulty, and not noticeably soft or enlarged. Pressure in the vaginal fornices provoked intense pain. The pouch of Douglas, with the pelvis in general, was filled with an irregular, resistant, and tender mass. The temperature was 101° F., and the pulse was 100. A tentative diagnosis of pelvic inflammatory disease was made and, accordingly, an operation was thought unjustifiable. At this time the amenorrhea was attributed to the x-ray exposure.

On October 3, under ether narcosis, a posterior vaginal incision was made. On entering the pouch of Douglas, a large quantity of serosanguinous material escaped, followed by a rather profuse hemorrhage.

The vaginal opening was packed temporarily with iodoform gauze. A free median abdominal incision was then made. On incising the peritoneum a small amount of fresh blood was found free within the peritoneal cavity. The uterus was

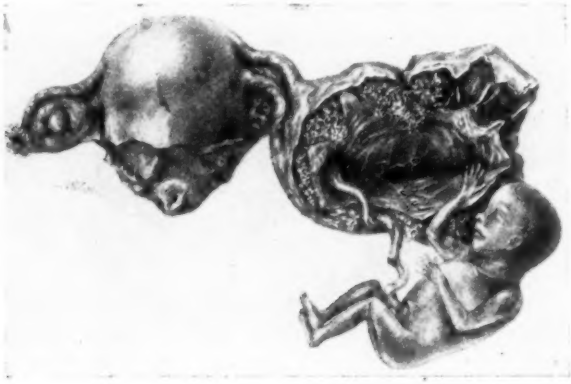

Fig. 1.

resting in the left side of the pelvis, apparently forced into this position by a large mass, which seemed to have its origin in the right tube or ovary. There were no omental or intestinal adhesions. The uterus, with the large mass, was delivered through the abdominal wound. The uterine body was studded with numerous fibroid tumors, and this organ, with the correlated mass, was removed. (Fig. 1.)

An examination of the specimen showed that the left tube and ovary were normal. The uterine end of the right tube was somewhat altered owing to the proximity of the gestation sac. The right ovary had been firmly compressed by the pregnancy and was almost completely destroyed. It was thought that the uterine myomas were in some way etiologically responsible for the extrauterine condition, since there was no other evidence of pelvic disease. It was altogether likely that the pregnancy began near or in the fimbriated end of the right tube, because there was no evidence of tubal rupture.

The placenta was freely attached to the posterior surface of the broad ligament and the right side of the pelvis.

The fetus, a male, nineteen centimeters in length, was well formed and probably in its fourteenth or fifteenth week of development.

The recovery of the patient was uneventful; she left the hospital in good condition twenty-eight days following the operation.

DR. LEONARD AVERETT, reported a case of **Accessory Uterus With Arrested Pregnancy.**

Mrs. V. P., referred August 31, 1926, gave a history of having aborted a three months' pregnancy on April 20, 1926, and while the fetus had not been seen to have passed, she nevertheless had bled profusely for ten days, passing organized tissue (presumably placenta) and large blood clots, and had suffered severe pain in the lower abdomen, intermittent in character. The uterus remained enlarged, corresponding in size to that of a three months' pregnancy. The patient was nineteen years of age; married one year; menstruation started at the age of sixteen; irregular (intervals of one to three months); three to four days' duration; not painful nor profuse.

Since the supposed miscarriage on April 20, she had been menstruating for about four days every two weeks, flowing profusely and passing clots for three days; her last menstrual period being August 27, 1926.

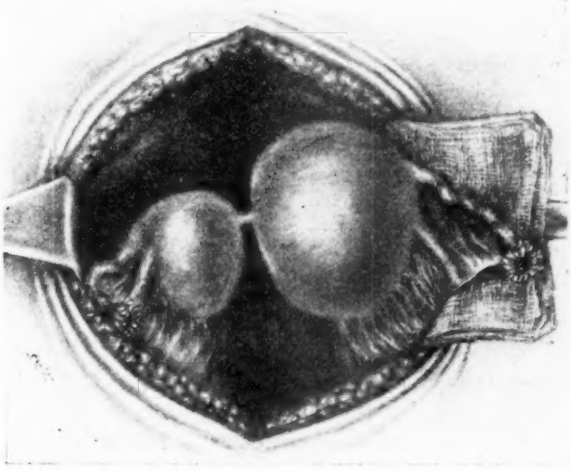

Fig. 1.

Examination showed the uterus symmetrically enlarged (corresponding in size to that of a ten weeks' pregnancy), rather soft, freely movable, and in the anterior position. No adnexal pathology or tenderness was palpable. Examination of the breasts, showed no change.

On September 21, the patient was sent into the Gynecologic Ward of the St. Agnes Hospital. Her chief complaint at this time was pain in the left lower abdomen and irregular vaginal bleeding. A vaginal examination disclosed findings different in character from those found upon the previous examination. The uterus was much smaller than normal, typically infantile in development, and pushed to the right; the right adnexae were not palpable. To the left of the uterus there was a mass about the size of a large orange, freely movable, rather dense, and very tender upon palpation. Taking into consideration its position, density, and regularity in outline, a diagnosis of dermoid cyst of the left ovary was made.

Patient was operated upon September 23, and there was found an infantile uterus with a right tube and ovary and a right round ligament; from the left

cornua (where one would expect to find the beginning of the left tube) there was a small band (about half an inch in length) at the end of which was a spherical mass, with the left tube and ovary arising from its uppermost left portion and the left broad ligament inserting into it. This mass was removed, conserving the left tube, ovary, and round ligament, which was sutured to the left cornu of the infantile uterus. (Fig. 1.)

Upon opening the mass, it was found that its walls consisted of well-developed muscle tissue, the entire cavity was lined with a placenta, and in the center was a fetus showing signs of having undergone maceration.

Patient made an uneventful recovery and was discharged from the hospital October 7, 1926. She is now menstruating every 28 days, a normal flow of four to five days' duration.

DISCUSSION

DR. GEORGE W. OUTERBRIDGE asked if the so-called accessory uterus had any separate cervix presenting in the vagina apart from that of the main uterus. In other words, what was there to prove conclusively that the mass was really an accessory uterus and not merely a somewhat atypical tubal pregnancy?

DR. ALFRED HEINEBERG wanted to know if the band which connected this mass to the uterus showed tubal tissue.

DR. AVERETT said there was evidence of a cervix in the accessory uterus, and there was no connection with the vagina, but there was a small opening in the band which connected the accessory uterus with the infantile uterus, and a fine probe could be passed through it. The predominance and compactness of muscle tissue differentiated it from a dilated fallopian tube. He could not demonstrate any endometrial tissue because the entire uterine cavity was covered with placenta.

DR. P. BROOKE BLAND, reported a case of **Dicephalus.**

The patient, twenty-eight years of age, had her last period February 10, 1926. She had one previous normal pregnancy and labor.

Following a period of amenorrhea, lasting from February 10 to the middle of May, 1926, the patient complained of slight irregular bleeding, combined with intermittent attacks of mild pelvic pain. This was regarded as a threatened abortion. The bleeding or spotting continued for almost three weeks and then gradually subsided.

During this time the patient was kept absolutely quiet in bed and under the influence of sedatives. From the middle of May until October 20, the day labor began, the general health of the patient was exceptionally good. At no time did she suffer with symptoms of toxemia, though for two months prior to delivery the abdominal distention was much greater than in her previous pregnancy.

Spontaneous rupture of the membranes was provoked, the patient stated, by straining while in an exaggerated stooping position. There was no other sign of impending labor. The patient was delivered three and one-half hours after active labor started.

The breech presented with the left foot protruding from the vulva. Efforts to extract the fetus were difficult. Finally the body and one head of the infant, a female, were delivered. Another head was noted in the pelvic cavity. After some manipulation the second head was delivered without special difficulty, although the patient sustained an extensive laceration of the posterior vaginal wall and perineum.

Owing to her favorable condition after the completion of the third stage, a primary repair was performed.

The fetus (Fig. 1), weighing 3280 grams, did not show serious signs of asphyxia. It was born alive, and inspiration and expiration were observed for more than a minute.

Fig. 1.

DISCUSSION

DR. GEORGE M. BOYD said he reported a similar case of dicephalus in 1901 from the Philadelphia Lying-In Charity Hospital. The patient had been in labor forty hours, the abdomen was irregular in outline, and the fetal heart was not heard. The cervix was dilated and the membranes ruptured. The head was presenting, well engaged. Without suspecting so unusual a monster, an attempt was made to deliver with forceps, but traction failed to advance the presenting part, and he thought the obstruction was due either to impacted shoulders or else to an amniotic hernia. A manual exploration of the uterus then revealed two heads attached to a common trunk. As the patient's condition did not warrant abdominal section, the uterus was emptied by first decapitating the head engaged and then performing podalic version. The well-nourished male fetus weighed 8½ pounds. Both heads were well formed, the extremities were normal, there were two hearts in one pericardial sac, and two aortae and pulmonary arteries. There were two spinal columns. The pelvis was single, and there were two ascending colons running parallel.

DR. NORMAN L. KNIPE, in 1912, had a similar case at the South Eastern service of the University.

The monstrosity had two heads, each normal in size and appearance, two

chests fused together, four arms and two normal legs, with a small rudimentary leg attached to the base of the spine.

The case was especially interesting because the mother had just given birth to a stillborn child, normal in appearance and size. The student in charge thought there was a twin child still to be born, but as it made no advance, he called a consultant. The consultant attempted version but failed. The patient was then sent to the University Hospital where a cesarean operation was done in preference to a difficult craniotomy. The dicephalic monstrosity was delivered, and the mother made an uneventful recovery.

NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY

MEETING OF APRIL 7, 1927

DR. A. F. HEBERT read a paper entitled **Hernia Funiculi Umbilicalis, with Report of Three Cases.** (See page 86.)

DISCUSSION

DR. HILLIARD E. MILLER had seen two cases of this sort. The first child, which had been delivered outside of the hospital, was brought in four hours later, after the hernial sac had ruptured, with four feet of small bowel lying free on the skin. The hernia was reduced and the abdomen closed, but death followed in five days, from peritonitis. The second case was seen in consultation, before delivery. The presentation was breech and the labor had been protracted. Delivery was effected without special difficulty, as far as the breech, at which point progress halted. Finally, after considerable traction, something was felt to give way, and it was thought a hip had been dislocated. An eight and a half pound child was eventually delivered, which presented a complete absence of the anterior wall of the abdomen. All the abdominal contents, stomach, liver, gall bladder, pancreas, small bowel, ascending and transverse colon, and appendix, lay on the outside. The child was much shocked, and though its heart continued to beat for some time, it never revived. There was no attempt at operation.

DR. HAROLD CUMMINS (by invitation) discussed these hernias from the standpoint of embryology. He pointed out that there are two grades, and that the minor grade represents simply a continuation or persistence of a limited herniation which is normally only transient. He exhibited specimens of normal feti, of approximately two months, and pointed out that at this time loops of ileum are pouched into the root of the umbilical cord, and are normally withdrawn into the abdominal cavity about the tenth week, whereupon the umbilical extension of celom is obliterated, just as the inguinal canal is closed after the descent of the testis. Any factor which prevents this withdrawal causes the minor grades of hernia. The more extensive hernias are associated developmentally with fissures of the anterior body wall and are not of the same genesis. He exhibited specimens showing extreme herniation of the latter type, and added that the child who had been exhibited by Dr. Hebert represented the same grade. He said that the origin of the more extreme cases is to be traced from the period in which the anterior body wall is in process of formation when all peritoneal contents are exposed directly to the exocelom. Closure of the cavity is finally effected through growth of the somatopleure and amnion, which extend progressively further towards the body stalk, until finally the amnion enwraps it completely, the former wide extra-amniotic communication thus being ultimately reduced to the culdesac in the

umbilical cord. Incomplete extension in this process is responsible for the major grades of umbilical hernia. The character of the eventration depends upon the location and extent of the defective closure of the body wall, and the development of this type of hernia is essentially different from that of the minor grade. The present view in embryology, suggested by the results of experimentation with the embryos of animals, holds that anatomically diverse defects, hernias, harelips, cleft palate, defects of the central nervous system, indeed any maldevelopment, may arise through the action of a single causative factor. Its selectivity in producing the defect is determined by the embryonic period in which the influence is exerted on the developing embryo. The vicious agent operates through the retardation of the normal rate of development, particular organs or regions suffering in accordance with the susceptibility associated with their state of elaboration at the time. An obvious corollary is that different agents may produce a like defect if their action be manifest at equivalent periods of development, the two being equally effective in retarding developmental processes. The cause of umbilical hernia is therefore to be sought among such factors as endometrial pathology or maternal toxemias, or similar generic mechanisms of retarded development.

DR. W. E. LEVY emphasized the importance of Dr. Cummins' remarks from the clinical side. The cord should be palpated carefully and tied at least an inch from the abdomen, as death might follow the inadvertent inclusion of a knuckle of bowel.

DR. HEBERT, in closing, emphasized the fact that prompt operation was the only means of saving these children, and that it should be done as soon as an operating room could be prepared, since after a few hours the formation of adhesions by the amnion and Wharton jelly made the procedure much more difficult.

DR. LEWIS H. LEVY reviewed **The Theory and Pathology of Ovarian Dermoids.**

DR. C. JEFF MILLER said that as torsion was fairly frequent during pregnancy and the puerperium, this should always be borne in mind as the possible cause of acute abdominal pain and associated symptoms at these times. He had recently seen an interesting case in which, eight days after labor, the patient had developed colicky pains over the abdomen, and some fever. A definite mass was attached in the region of the gall bladder, and some upper abdominal pathology was suspected. Operation at the end of a month, showed a dermoid attached to the liver; it had apparently been carried upward during pregnancy, become twisted during delivery or in the early days of the puerperium, and its pedicle had become sufficiently attenuated, as involution occurred, to reach down to the pelvis, leaving the body of the cyst attached to the liver. He had also seen a case in which the dermoid was attached exactly under the umbilicus.

DR. HAROLD CUMMINS remarked that teratomata possess some features which are common to artificial cultures of embryos. In the latter the components vary in accordance with the origin of the stock, and under suitable conditions attain an abortive organization. A teratoma, in his opinion, might be regarded as a culture developed under conditions which are unfavorable to proper organization of the embryonic parts. A teratoma differs from tumors generally in that it originates from a cell possessing more comprehensive potencies of differentiation. On account of this possession, the parent cell might be considered a germ cell, but the occurrence of such varied degrees of development of the product suggested that this definition was not strictly necessary. In his opinion it was difficult to conceive of the universal application of the blastomere theory.

DR. PETER GRAFFAGNINO reported two cases in which a dermoid complicated pregnancy. The first patient, five months' pregnant, was admitted with apparently

the symptoms of acute appendicitis, although the temperature was not elevated, and the blood count was normal. A normal urine eliminated pyelitis, and while the patient was being observed, the condition cleared spontaneously. Three days later, without warning, a similar acute attack occurred, complicated by a considerable degree of shock. Immediate operation revealed an ovarian dermoid with a twisted pedicle, quite gangrenous. It was excised, and her recovery and the ensuing delivery were without incident. The second patient furnished a rather vague history of a six months' pregnancy, although examination disclosed her to be but three months' pregnant. Her symptoms suggested appendicitis, but a large mass in the upper abdomen led him to believe the condition to be an ovarian cyst with twisted pedicle. X-ray confirmed the presence of two distinct tumors, and operation revealed a dermoid, with twisted pedicle. This recovery was also uneventful. Both cases, he thought, emphasized the necessity of bearing in mind this condition as a complication of pregnancy at any stage as well as of the puerperium.

DR. MAURICE J. GELPI read a paper entitled **Rupture of the Uterus in the Scar of a Previous Cesarean Section, Occurring Twice in the Same Patient within One Year.** (See page 85.)

DISCUSSION

DR. PETER GRAFFAGNINO quoted the figures from Charity Hospital, which showed that in the last 11,516 cases delivered in that institution, rupture had occurred thirty-one times, an incidence of about one in every three hundred seventy-one cases, including all types, spontaneous as well as postoperative. The usual incidence of 2 to 4 per cent quoted for rupture after cesarean section suggested again the question of how to deliver a woman previously delivered by cesarean section. Reports in the literature of women who had had as many as eight subsequent spontaneous deliveries after the first cesarean delivery, and particularly reports of podalic versions and protracted labors after operative delivery, persuaded him that provided proper precautions were taken, delivery in hospital, under close scrutiny, furnished a sufficient margin of safety for the patient. In contracted pelvis, of course, there was no option but to repeat the cesarean. He pointed out that since about a fifth of all ruptures after cesarean section occurred between the seventh and eight months, the fallacy of depending only on a second cesarean to avert this catastrophe was apparent.

L. L., a colored woman, was admitted to Charity Hospital at the beginning of the eighth month of her tenth pregnancy. The previous nine deliveries had been spontaneous, and the puerperia all afebrile. Labor began some three weeks later, and was quite normal, though progress was rather slow. Because the patient's previous history was so well known—indeed she was a hospital character—the interne paid very little attention to her. Finally, late in the afternoon, when the head was down on the perineum and the cervix was fully dilated, he gave her two minims of pituitrin. Almost immediately afterwards he was informed by the nurse that the patient was badly shocked and bleeding profusely. He had left her with the head on the perineum, now he found it retracted, and the child definitely palpable under the abdominal wall. The diagnosis of ruptured uterus was clear, and Dr. Graffagnino was summoned at once. When the bladder was catheterized in the operating room, no urine was found, only pure blood being obtained, so that it was clear that the bladder had ruptured also. Immediate laparotomy revealed a dead fetus free in the cavity, as was the placenta, a rent in the uterus on the right from cervix to fundus, and a rent in the bladder at least five inches long. What to do was a problem, since the patient had been repeatedly examined during the course of her labor, and urine had been spilled into the abdominal cavity, so that there was no doubt of infection being present. A rapid Porro hysterectomy was done,

the wound in the bladder was sutured with chromic catgut and a final layer of linen, and a Pezzer catheter was inserted. The peritoneal cavity was closed by suturing the parietal peritoneum to the peritoneum reflected on the uterus posteriorly, and a drain was left from above, extraperitoneally. Thus, if infection were inevitable, it would take place outside, since all infected parts had been treated extraperitoneally. Convalescence was without incident for three weeks. Then the bladder sloughed and a urinary fistula was evident in the abdominal wall. This gradually closed, and she has recently been discharged in excellent condition.

DR. L. A. LEDOUX inquired whether it were definitely known in what percentage of ruptures infection was a factor in the production of the condition. He cited a case of his own, recently reported, in which after a smooth recovery a rupture of the uterus developed on the tenth day, and autopsy revealed the infection to be originally intrauterine. In his opinion this illustrated the point that infection was the prime factor in reducing the strength of the operative scar, and that, when once it had set in, the method of suturing had nothing to do with the final outcome, since no type of sutures would hold together an infected and necrotic wound.

DR. GELPI, in closing, said that Dr. Graffagnino's figures, which included all types of rupture, naturally could not be compared with those he had quoted, which included only ruptures after cesarean section. The figures would naturally be much higher now, since ruptures were more frequently reported, and since the increased incidence of cesarean section naturally increased their incidence. He believed that no more appalling intraabdominal pathology could be seen than was found in this type of case, even after spontaneous rupture, and he cited an instance of spontaneous rupture in which the patient was brought in with six or eight feet of intestines protruding from the vagina, death occurring on the table before the abdomen was even opened. He had not the figures at hand to answer Dr. Ledoux's inquiry as to the part played by infection, but he believed that certain authorities insisted that infection was at the basis of every rupture, whether it was recognized or not. In his own case the patient's story of her first operation naturally led to the assumption that infection was responsible, at least for the first rupture. He believed that in his management of the case he was open to criticism on two counts. He had used but two layers of sutures, as was the custom then; since that time he had used three, though he was not sure that the additional layer did anything beyond adding to the surgeon's own peace of mind. In the second place, possibly he should have been more radical at the first operation. His excuse was that he was primarily concerned with saving the patient's life, rather than guarding her against possible uterine ruptures in the future. He could sew up a rent in the uterus faster than he could do a hysterectomy, and her condition was such that every moment of time was vital.

CHICAGO GYNECOLOGICAL SOCIETY

STATED MEETING, MARCH 18, 1927

DR. A. H. CURTIS presented a report of a case of **Pregnancy After the Menopause.**

The patient, forty-six years of age, complained of symptoms suggestive of ulcer of the stomach, great fatigue, and prostration. She was worn out, mentally and physically, and felt as though she were growing prematurely senile. She gave a history of five pregnancies, with two living, healthy children. Menstruation ceased three years before and had not returned.

Upon examination he found a tumor rising out of the pelvis to the level of the navel. This tumor, together with other evidence of a typical character, made certain a diagnosis of normal pregnancy. The x-ray picture, yielded corroborative testimony. It is rare to see pregnancy in a woman of forty-six, and still more so, a pregnancy three years after supposed menopause.

DISCUSSION

DR. N. H. HEANEY recalled one case of pregnancy after the climacterium had evidently been safely established. A school teacher in middle life came into the service of Dr. Webster, stating that she had the climacterium three years before. She had a cystic tumor of some size, which proved to be a pregnancy as shown by the x-ray.

DR. J. B. DELEE presented an **Electric Clock** which strikes every fifteen seconds. Similar clocks have been in use at the Chicago Lying-in Hospital for ten years but it has been rather difficult to popularize them because of the cost, $175.00. This clock was invented by Dr. Wachenfeld, of Sweden. It is an ordinary Big Ben alarm clock in which there is an electric ringing apparatus. It costs about $40.00. With the head stethoscope on, all that it is necessary to do is to wait until the bell strikes and then start to count.

DR. J. B. DELEE reported a case of **Tubouterine Pregnancy.**

The patient was in her third pregnancy. The last period occurred on December 22. Shortly after the period began she had great pain in the right side of the abdomen, which increased in severity until the time she came under observation. It was the pain that brought her to the doctor rather than the thought that she might be pregnant. Examination showed the uterus with a tumor mass in the right side, and it was diagnosed an extrauterine pregnancy by Dr. DeLee, while his associate, Dr. Horner, diagnosed the case as pregnancy in a horn. At operation they found that the woman had what was first taken to be a double uterus. The portion of the tube in the uterine wall was distended by the pregnancy, and the cavity of the uterus also formed a part of the gestation sac. The distended tube went into the uterine cavity. Its wall was so thin that one could almost see through it, showing it was not an ordinary angular pregnancy.

DISCUSSION

DR. A. H. CURTIS asked if Dr. DeLee meant an interstitial pregnancy. He did not see the object of dividing interstitial pregnancy into subgroups. Approximately only 100 cases have been reported.

DR. DELEE, in closing, said that an interstitial pregnancy does not extend into the cavity of the uterus. It extends outward. A tubouterine pregnancy can develop into the cavity of the uterus and terminate normally. He had had no experience with that type. In this case the cavity occupied by the ovum was composed of the tube and half the uterus. Werth and Kuestner report similar cases; it is, therefore, a proved clinical entity.

DR. A. H. CURTIS presented a specimen of **A Malignant Corpus Luteum Tumor.**

The patient, fifty-seven years old, was operated upon one week previously for a tumor which rose to the level of the umbilicus. She had bleeding during recent months, which made one think first of a malignant growth, but the bleeding was somewhat periodical and like a return of menstruation. Upon opening the tumor, Dr. Curtis found it was filled with blood. The tumor substance was of a very

decided yellow color, like a suprarenal gland or corpus luteum. Microscopic study revealed acini which simulated the structure of suprarenal tissue or corpus luteum, which look so much alike that they cannot be distinguished. He believed this to be a malignant corpus luteum tumor and that these growths are not so rare as has been believed heretofore.

This was the third tumor of this type which he had seen, one being in a girl of nine.

DR. BARTON COOKE HIRST, of Philadelphia, presented, by invitation, a paper entitled **Ovarian Dysfunction Dependent on Abnormalities of the Ductless Glands.** (See page 79.)

DISCUSSION

DR. A. H. CURTIS said this field of investigation was one which no single individual or group of individuals could follow out alone. It required the untiring labors of a number of men in order to accomplish anything of notable value.

He presumed every one advocated, in operations for fibroids and diseased tubes, the presentation of sufficient endometrium to assure some menstruation. But what is to be the attitude toward conservation of ovaries in those instances in which disease of the cervix necessitates complete hysterectomy? Frank has demonstrated that the ovarian hormone is present in the circulating blood prior to each menstruation and is excreted with the normal monthly flow. But in young patients who are deprived of a menstruating uterus the preservation of ovaries is followed by monthly accumulation of noxious waste products. Despite this recent evidence, Dr. Curtis' present attitude is inclined toward conservation of healthy ovaries in young women subjected to total hysterectomy.

DR. C. W. BARRETT asked Dr. Curtis if, in spite of the great many cases of hysterectomy with one or both ovaries removed, he would be inclined to recommend Dr. Frank's suggestion that the ovaries be removed when the uterus is removed. It seemed to him there are many clinical evidences to show that a woman is very safe and rather more comfortable with the ovaries left than with the ovaries removed.

DR. HENRY SCHMITZ said he had been very fortunate in obtaining standardized ovarian extract, and his observations coincided with those of the essayist.

A patient who had a full-term labor about four years ago was worried because she had not become pregnant again. Menstruation was perfectly normal though scanty. A hypofunction of the ovaries was probably the cause of the sterility. The ovarian hormone was administered subcutaneously, and within two weeks following the last menstruation and four weeks after beginning of treatment, the patient became pregnant.

Another patient, twenty-four years of age, had had a bilateral ovariotomy. Marked symptoms of a menopausal character appeared, rendering the patient an invalid. In this instance he gave the hormone and the symptoms disappeared entirely within four weeks.

He had never been able to secure similar results with the hypodermic use of any other ovarian extract.

DR. A. H. CURTIS said it would be interesting to know what Dr. Hirst had to tell as to the helpfulness of corpus luteum preparations which have been so much used in efforts to overcome the toxemias of pregnancy.

DR. HIRST, in closing, said his excuse for this rather inconclusive presentation was a desire to stimulate as many physicians as possible to try this sex hormone so that some conclusion might be arrived at. As Dr. Curtis said, the observations

of two or three physicians meant nothing. It required collective investigations. The sooner a conclusion is reached, the better for the physician and for his patients, whether it is favorable or not.

Another idea he had in mind was to awaken the clinical laboratories to the necessity of testing the blood for the presence and the amount of the sex hormone. He knew of no clinical laboratory that is prepared to do this at present, except perhaps that of Dr. Robert T. Frank at Mt. Sinai Hospital in New York. It is becoming a matter of importance. For example, suppose a young nulliparous woman or a sterile woman shows evidence of underdevelopment, and the physician wishes to know if the uterus only or the ovaries also are at fault. It would be highly important to determine the functional activity of the ovaries. If the uterus is shrunk or underdeveloped, it can be helped by electric stimulation; if the ovaries are not functioning, the sex hormone can be used in addition.

In answer to Dr. Curtis' question in reference to the sex hormone, he said why not let not only the ovaries but some endometrium remain. Howard Kelly advocated this procedure years ago. It seemed reasonable, and the speaker always endeavored to carry it out. If a complete hysterectomy is not required, he always tries to leave enough endometrium to assure the patient that she has not been mutilated. He had knowledge of three patients who are in insane asylums from brooding over their mutilation. If some endometrium is left in these patients with an ovary, the woman will menstruate perhaps scantily but enough to make her feel that her sexual life is not permanently ended.

DR. J. P. GREENHILL presented **A Human Ovum Approximately Nineteen Days Old.***

Correspondence

Toxemia of Pregnancy, a Touch of Patience and a Grain of Sense

To the Editor: We have just read a spirited article written by E. M. Lazard of Los Angeles, California, entitled, "Is Magnesium Sulphate Intravenously Warranted in Eclampsia? Clinical Results vs. Experimental Evidence." (AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, June, 1927.) Previously we had been tremendously interested in Stander's work, with part of which this article deals inexorably, and had been fascinated by the paper entitled, "The Toxemias of Pregnancy and the Treatment of Eclampsia" published by J. Whitridge Williams in the *Journal of the American Medical Association*, February 12, 1927, in which the author, among other expressions of opinion, stresses the present Hopkins classification and reports a mortality of less than 2 per cent in 54 so-called mild eclamptics under the Hopkins modification of the Stroganoff treatment.

I lay no claim to be an authority on the toxemias of pregnancy, but only to a reasonable interest in the subject, which has driven me for fifteen years to see personally every case of toxemia of pregnancy possible, working in a clinic which, during this period, has cared for between 1100 and 1200 "toxemic chronic nephritic group cases." I have been chairman of a committee of the Obstetrical Section of

*The clinical aspects of this study appeared in *Surgery, Gynecology and Obstetrics*, October, 1927 and the histologic study of the ovum appeared in *The American Journal of Anatomy*, November, 1927.

the Massachusetts Medical Society which analyzed a small series of four hundred collected cases. In the course of these fifteen years, not counting odds and ends of carefully studied personal material, I have studied three series of approximatly four hundred cases each in some detail.

To show the spirit in which the following comment is made I will quote myself in a talk on toxemia made recently in Williamstown, Mass. I said in substance commenting on Stander's and William's work, "Though there are many points in their work on which we must for the present disagree, none the less this subject of toxemia has us all so baffled and at a standstill that we cannot afford to be in anywise acrimonious or dubious among ourselves. We must accept and analyze with great care and fairness the work of all sincere students of that most fascinating and little understood problem of obstetrics."

In the light of my own experience and study, for example, no statement could be more ridiculous and more arbitrary at first sight than that preeclampsia represents only 5 per cent of the toxemic chronic nephritic group cases because, in our three series of four hundred cases each, the first showed 25 per cent convulsive toxemics, the second showed 50 per cent convulsive toxemics, and the last series of similar number showed 8 per cent of convulsive toxemics. Since this high proportion of these twelve hundred cases had eclampsia, we must agree that they had preeclampsia; yet on closer analysis it may well be that hospitalization in these groups only took place in such severe toxemias that this percentage of convulsive toxemics supervened and on this reasoning that Standers and Williams are right.

Again Lazard's detailed cases in his last article in which he attributes the delivery of a live child to the use of magnesium sulphate over rather prolonged periods in four cases, mostly chronic nephritics, is totally unconvincing to us. In a study we made four or five years ago under title, *Recurrent Toxemia of Pregnancy,* cases of this sort with this outcome repeatedly occurred, and this long before we ever used a dose of magnesium sulphate intravenously or intramuscularly. Yet here again further thought may make this use of the drug more convincing in this respect.

Our own small experience with magnesium sulphate intravenously (perhaps in 150 or 200 cases) has seemed to show that in the true toxemias of pregnancy it did lower blood pressure to a useful extent, but that in chronic nephritics the blood pressure dropped only temporarily or not at all. This to such a degree that we have felt that it was almost a sure diagnostic differentiation in doubtful cases.

Further, there is no question but that Stander's and William's point of view about "low reserve kidney" and their explanation thereof leaves us colder than any other detail of toxemia which has ever been presented. The Eden division of eclampsia into severe and mild is the next most unreasonable proposition we have met. At first glance, as we have seen eclamptics, they were all severe, and once fits have occurred, we have been unable to make a satisfactory prognosis and doubt very much if others can make a better one than ours. Everything in our experience makes us feel that the only way we could classify eclampsia as severe or mild would be after each patient died or got well, by which time it is of little therapeutic importance. Yet here again we may be wrong; the term "low reserve kidney" may really mean something, and the Eden classification may give us a divisional grouping for better treatment. One explanation of our divergent views occurs. Perhaps there are geographic differences of eclampsia. Perhaps on this basis we do not see "Russian eclampsia" or "Baltimore eclampsia" or even "Los Angeles eclampsia." Another thought, perhaps in other places convulsions are allowed to develop in cases under care because of a more conservative point of view about interference than we hold, and since there has been time to study these cases a more accurate division into severe and mild may be truly made.

For years with my colleagues, in my teaching, and above all in my own thinking

to myself on obstetric subjects, I have urged one point of view, namely, that we should differentiate the things that we think we know from the things we actually know. To think with Lazard that a single drug will influence the known progression of nephritis in pregnancy or the known irregularity of these progressions, or to think, once having seen at autopsy a dead eclamptic, that you can stop the definite progress of the disease without removing the cause, is to admit to an unbiased observer that too great enthusiasm to partial results have been aroused in an individual.

So much for the healthy scepticism of a person who feels that it is more profitable to attempt to reconcile our ideas than to disagree.

Now let us take the other outlook. The work of Stander in relation to the placental exchange of fats, in relation to the acidotic group of eclamptics and deoxygenation, in relation to the CO_2 combining power of the blood in these cases, and with morphia, is splendid work. His work on all inhalation anesthetics in their production of eclamptic-like lesions (and this leads toward delivery of eclamptics under some form of local anesthesia) is, I believe, the most splendid single scientific contribution to this subject which has been made, and checks well with our own clinical observation.

Lee Dorsett's wonderful series of eclamptics treated only with magnesium sulphate intramuscularly together with the work of Lazard and others have shown at least that magnesium sulphate is nearly always a controller of eclamptic convulsions and that is all that it has shown and that is of great importance.

Williams' and Stander's classification even if not final is a great step in the right direction and is based on sound, painstaking scientific work which is more than may be said for any previous classification.

The use of large amounts of fluids, and glucose and insulin in the acidotic group, and perhaps concentrated glucose intravenously in the anuric group, are sound assets.

The discovery of blood chemistry and its application is in the end an answer to the etiology. Finally, the abandonment of divulsion of the cervix and delivery, so that now at least by the Stroganoff method and its modifications we allow such eclamptics as are destined to live, to live, is a wonderful advance.

These are all results of the work and thought of the last few years. We are getting together a real armamentarium, and the cyclic treatment of toxemia is over.

The thought is this. Let us accept the little bit of truth each of us brings. Let us try to reconcile our views and not acrimoniously debate detail. Let us above all not intensify the old fashioned difference of viewpoint of the clinician and the worker in the laboratory—each has much to learn from the other. Only by cooperation and some overlapping in knowledge can our toxemic problem be settled. I have always been a straight clinician, and yet the work of Stander and contact with the biologic chemist of our own hospital has in the last two years given me a knowledge and a command of clinical possibilities in toxemia never before possessed and never possessable by any amount of straight clinical observation.

Toxemia now is the obstetrician's unconquerable enemy in spite of all optimism. Fifty per cent was the maternal mortality in the Massachusetts series mostly done by obstetricians of merit in hospitals of excellent sort. None of the obstetric professors who cry that they have not enough cases of eclampsia to teach their students have yet a leg to stand on except that the hope is the father of the thought.

In conclusion then, I know, on the basis of the experience cited above, one thing about eclampsia and that is this: I know that in two parallel series of four hundred cases each of the "toxemic chronic nephritic group," we had in the first a mortality of 25 per cent in the convulsive toxemics, and we had in the second, partially under Stroganoff's method and magnesium sulphate treatment,

a mortality of 24 per cent in convulsive toxemics, practically the same. In the first series we had 25 per cent of convulsive toxemics and in our second series of equal size 8 per cent of convulsive toxemics, and that, therefore, by count in a series of four hundred women in this group we saved thirty actual lives by interfering earlier before convulsions than in the first series. By this result I feel justified in stating that until somebody demonstrates the cause of toxemia of pregnancy and the definite therapeutic means of removing this cause, that since eclampsia occurs only in pregnant women, interference with pregnancy prior to convulsions is the main therapeutic agent at our command, and we urge that until this happy result has been obtained by laboratory methods, which surely is the manner in which it will be obtained, we should adhere to this sound clinical principle and should not be led astray, especially by the report of a small series of clinical results with the use of any single therapeutic agent.

The conquest of the toxemia of pregnancy depends primarily on a universal acceptance in this country of some index, of some classification, some cooperative mode of study in every great obstetric center—Baltimore, Los Angeles, St. Louis, Ann Arbor, Chicago, Philadelphia, New York, Boston, and all the rest of our obstetric units. This is not an idealization. Tangibly it means this. We urge strongly that a committee of representatives of the great obstetric societies of the country meet with a view to establishing a working index and classification, tentative at first and changeable at each yearly meeting. It is only in this manner, with the cooperative spirit of the best obstetricians of this country, with the personal exchange of ideas, that we can take advantage of blood chemistry and the other scientific laboratory knowledge and finally, after some years of understanding and helpful effort accomplish the result. I urge this on all specialists in obstetrics in the United States and Canada as a most obvious and reasonable basis for real results.

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19 BAY STATE ROAD, BOSTON, MASS.

To the Editor:

Dr. Edgar F. Schmitz has published in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY (xiii, No. 6), a paper about a very interesting case of endometrioma in the ovary and inguinal canal. He gives a new theory for the explanation of these parts of the ectopic endometrial tissue, which grow outside of the abdominal cavity and are, therefore, not to be explained by Sampson's implantation theory. He suggests that the glands of these parts of the endometrioma are derived from metaplasia of the endothelial cells which line the finer capillaries and lymphatics. Fig. 7 illustrates this metaplastic transformation.

I published a paper entitled "zur Frage des ektopischen Endometriums" ("The Question of the Ectopic Endometrium") in the *Archiv für Gynäkologie* (vol. cxxvii), in which I gave the theory of the metaplastic or prosoplastic transformation of the endothelial lining of lymph spaces into columnar epithelium which leads to the transformation of the lymph spaces into glands of endometrial type or into ectopic pseudoendometrium (pages 587 and 607). This is illustrated by some figures of which especially No. 23 harmonizes with Fig. 7 of the article by Dr. Schmitz.

For the preservation of my priority, I want to state that my paper was finished in August, 1925.

WALTER SCHILLER, M.D.

VIENNA, Aug. 16, 1927.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Collective Review

New Books

BY ROBERT T. FRANK, A.M., M.D., F.A.C.S., NEW YORK CITY

OF GENERAL INTEREST

Volumes II and XI of the *Medical Department of the United States Army in the World War*[1] form two huge tomes. The contents of these volumes are of utmost interest to all medical men and will bring back both pleasant and unpleasant memories to those of us who formed part of the Medical, Veterinary or Sanitary Corps of the army.

These volumes are important and worthy of careful study, particularly by the younger practitioners who might at some future date be called upon to take part in military activities. If, as we all hope, many years elapse before a new war in which we are involved occurs, doubtless many changes in technic and procedure will again be necessary. But for the next decade or more, unless the site and type of military operations are in a quite different field, the observations made from 1917 to 1918 should prove of utmost value. It is largely for this reason that I submit a somewhat detailed review.

Volume II covers the administration of the American Expeditionary Forces. It was prepared under the direction of Major General M. Ireland, Surgeon General, with the aid of an editorial board consisting of both regular army officers as well as medical men who entered the service during the emergency. In spite of the huge size of these volumes, extreme compression was necessary, as the amount of material on hand was overwhelming. The evacuation service as well as most of the sanitary service will be found respectively in Volumes VIII and VI. For the sake of brevity, only one hospital center is described. Careful reading of the volumes cannot fail to impress one of the very fair and impartial description of the difficulties, problems, uncertainties, and mistakes encountered and made, with the result of disarming any adverse criticism which any of us may feel inclined to offer.

American medical observers were sent to Europe early in the War during the year 1914, and later on a more numerous personnel was sent to the various armies for observation. It is to be regretted that, in spite of their presence and presumably in spite of their reports, so little advantage was taken of the change due to modern conditions

[1]**The Medical Department of the United States Army in the World War.** Volumes II and XI. Major General M. W. Ireland. Government Printing Office, Washington, 1927.

in instructing medical officers at the training camps. I personally was at one of these camps for five months, during which time the newest information received on medical subjects dated from the Civil War, except for lectures delivered by other inmates of the camp whose ignorance of modern problems was as abysmal as my own. Only one *line* officer of the Canadian forces talked to us on conditions in the trenches.

Selection of a few of the most important items is difficult because of the wealth of material dealt with. Casual officers assigned to the British were hard to keep track of. We constantly averaged 800 officers, 600 nurses and 1,100 enlisted men with the English service. A certain degree of uncertainty as to the exact location of men, officers, nurses and enlisted men in our own expeditionary forces is acknowledged. This was due to many causes and resulted, as I personally can vouch for, in confusion and individual hardship. By January 11, 1919, 17,767 medical officers, 9,994 nurses and 145,815 enlisted men comprised the Medical Corps of the American Expeditionary Forces, a total of 173,576.

The machinery of promotion, as we all were well aware of, presented unexpected difficulties, and proved most unequal. This applied particularly to those assigned to the British Forces. Very few promotions were made in the American Expeditionary Forces in the first ten months of service, and few after November, 1918.

Lack of space prevents me from discussing the dental and nurses' service.

Many pages are devoted to the laboratory service and that of infectious diseases, as well as epidemiology. Description of construction and administration of base hospitals is gone into in great detail. One hospital center is likewise described at length. The field and mobile hospitals, our hospital trains, are also discussed, but evacuation hospitals are dealt with in another volume.

The autopsy service was found very insufficient, largely for lack of trained pathologists, as many of the bacteriologists were needed for the study of infectious diseases, wound bacteriology, water examination, etc. By June, 1918, permission for preparing beds for 15 per cent of the A. E. F. had finally been accorded.

Some confusion resulted from the appointment of "directors" of professional services. These were not informed of either their powers or the limitation of their field. Eventually, x-ray, orthopedic, eye service, neurologic service, and surgical teams were established. These surgical teams supposedly consisted of an operating surgeon, an assistant, an anesthetist, two nurses, and two corpsmen. My own surgical team functioned with a single nurse borrowed at random whenever possible, although, finally, one week after the armistice had been declared, a single nurse was assigned to me. The two corpsmen assigned to me for five months' service in the evacuation hospital, doubtless were efficient truck drivers in Detroit (their pre-war occupation), but proved a liability instead of an asset as assistants, mainly keeping me occupied in trying to prevent them from being A. W. O. L. and out of the clutches of the court martial, which I actually succeeded in doing until after the armistice was declared.

The maxillofacial service was greatly handicapped by lack of equipment. The venereal and skin service treated a large number.

The medical service had to deal with tuberculosis, psychiatric cases, communicable diseases and gas poisoning.

The medical supply service had a huge task to accomplish in the face of tremendous difficulties.

Over 262,000 personnel of all branches formed the American force in Germany by January, 1919. Here the Medical Department had to contend particularly with the diseases suffered by the civil population, especially influenza, typhoid, and diphtheria. The sudden influx of troops doubled the number of local inhabitants in the occupied area and grave emergencies arose before it was possible to adequately control the water supply and disposal of waste. The infestation by lice likewise proved a difficult problem to contend with.

Volume XI deals with general surgery, orthopedics, and neurosurgery. It was hoped to be able to obtain the final results in peripheral nerve injuries but this very valuable study had to be abandoned because of the rapid dispersion and amalgamation into the civil population.

The surgeons in the great war were confronted with an entirely new problem due to the new pointed rifle missile which produced an area of devitalized tissue throughout its course. This new problem was met by the allies long before our entry into the war by the procedure of débridement, which consisted of excision of the surrounding injured area, followed by primary or secondary suture. The treatment of shock was greatly improved by transfusion and heating of those patients whose temperatures were subnormal. My own personal experience and that of others in evacuation hospitals showed that the gum salt solution was of no value and, in fact, in many cases, did actual harm.

The war showed the importance and value of armor, especially of helmets. Some interesting chapters on artillery and small arms are found in Volume XI.

The briefest summary of casualties is of interest. Of lacerated wounds, 46,549; penetrating wounds, 42,374; fractures, 25,272; total injuries sustained in battle, 153,537. Death from wounds received in battle, exclusive of deaths on the field, amounted to 12,470. The number of discharged for disability resulting from battle injuries were 22,330. Incomplete statistics going to July 11, 1921, show the tremendous number of over fourteen and one-half million days lost in hospitals.

Surgery at the front includes the treatment of wounds on the field and in the various hospitals of the advanced area. In the American Army no preferential treatment was accorded to the lightly wounded but it was found that many of these could be evacuated to the rear areas without incurring undue danger from infection by the gas-forming bacilli. Consequently our evacuation hospitals dealt especially with the more severely wounded whom it was not deemed advisable to send unoperated to the rear. I can personally vouch for the fact that during the rushes we frequently evacuated the recently operated patients before they were quite out of their anesthetic. In the hospital with which I was connected during the Chauteau Thierry offensive, we evacuated continuously for days and regularly as often as three times in twenty-four hours. This condition is also mentioned in the text.

The conference on problems relating to the area of advance in

Chapter V, giving a discussion by many of the consultants, is most interesting. The same applies to the answers to the questionnaires, although the opinions advanced by no means settle these questions finally. The question as to "in what cases gas and oxygen is especially indicated?" appears rather amusing when I recall that during five months in an evacuation hospital I never saw a cylinder of nitrous oxide. In this questionnaire the gum salt solution, previously referred to, did not receive favorable comment.

Anesthesia, wound shock, localization and extraction of foreign bodies under x-ray control are all of interest. In reference to the last I wish to put in an additional word of praise for the extreme, unselfish devotion which a large number of x-ray men showed throughout the tremendously long and trying hours of their daily work. The wonderful accuracy with which they localized innumerable foreign bodies, often multiple in the same patient proved admirable, so that if the body was not found at the place indicated, we felt the fault was more often ours than that of the radiologist. Considerable space is devoted to the dreaded gas gangrene. Tetanus, because of routine prophylactic injections, proved a negligible factor by the time that our armies entered the zone of activity, only 36 cases being reported, a rate of 0.014 per thousand. Chapter XII deals with wounds of the soft parts, especially with débridement. The next chapter takes up joints. After this, wounds of the chest, abdomen, genitourinary tract, and long bones are discussed.

Section 2 of Volume XI deals with orthopedic surgery, covering all portions of this field, including appliances and treatment of amputation stumps. The final section of this volume deals with neurosurgery, which does not lend itself to review but contains a tremendous amount of valuable information.

Four contributions from the Division of Medical Education of the Rockefeller Foundation have come to hand, dating from the year 1924 to 1927. They deal with *Methods and Problems of Medical Education.*[2] The publications give brief descriptions of clinics, laboratories and methods of teaching in different parts of the world, with the aim of assisting those who are planning improvements in building and methods.

Such varied subjects as the sanitary survey as an instrument of instruction in medical schools (Milton J. Rosenau), as well as a sanitary survey of Rochester, New Hampshire (S. Warren), are contained in the second series. The fifth series contains many contributions from Washington University, St. Louis, covering the departments of anatomy, pathology, bacteriology and public health as well as physiology. McGill University, Montreal, has descriptions of some of these same departments, as well as those of botany, zoology, biochemistry, pharmacology and the O. P. D. Numerous other contributions from as diverse regions as Soochow, China; Utrecht, Netherlands; and Montpellier, France, are included.

Series 6 is equally international. Among others, articles from Peking, China; London, England; Dublin, Ireland; Milan, Italy, etc., have been incorporated. The subjects dealt with are departments,

[2]**Methods and Problems of Medical Education.** Second series, 1924; fifth series, 1926; sixth series, 1927; seventh series, 1927. Division of Medical Education. The Rockefeller Foundation, New York.

buildings, equipment, and even details of teaching, as those of percussion in Vienna and visual instruction in Germany.

The final series published (No. 7, 1927) deals entirely with the new medical school in Rochester, New York.

These contributions cover so many subjects that they do not lend themselves to review. Anyone planning to change and improve a medical school cannot fail to obtain a tremendous amount of valuable information from their pages.

The New Medical Follies by Morris Fishbein, editor of the *Journal of the American Medical Association*,[3] is a cleverly written, caustic, striking, fearless exposition of the many medical cults and foibles which exist, especially in our country. The treatment is somewhat journalistic, which is explained by the fact that many of these essays have appeared in lay journals as well as in medical publications. The author brings out that the cults scrupulously avoid all the fundamental sciences. In alphabetic arrangement he gives a short but complete survey of all the cults, beginning with "aerotherapy" and ending with "zonotherapy." This will be of use as ready reference to those who wish to look up some particular cult. He then takes up beauty parlors, the beauticians and cosmetologists, etc., who occupy at least 2000 "Shoppes" in New York City. Next to be roasted are the licensed advertising plastic surgeons and the reduction and dietary fads. Rejuvenation can be summed up by the aphorism, "There is no fool like an old fool." Such outstanding figures as Steinach, Benjamin, and Voronoff are pilloried. The autointoxicationists, at the head of whom is Arbuthnott Lane, do not escape. A separate chapter is devoted to the rise and fall of electicism and, in conclusion, Fishbein "pans" the exaggerated tendencies of the psychoanalysts whom he includes in the cultist movements. The book is well worth reading and contains many unvarnished truths.

GYNECOLOGY

Biologie und Pathologie des Weibes,[4] edited by Halban and Seitz, is slowly approaching its completion. Of the eight volumes, nearly seven and one-half are completed, leaving only one and one-half volumes to be published in the near future.

Installment 34 contains four different subjects. Sigwart here concludes his pathology of the puerperium. As the literature is so tremendous, he has attempted to sift the material, giving the views with which he is personally most familiar. The treatment of puerperal sepsis he divides into local and general. As a routine in the presence of infection he lays open all perineal and vaginal wounds. He is strongly opposed to intrauterine irrigation, which is both dangerous and useless. He fears digital exploration of the uterine cavity even more. On the other hand, he believes in early serotherapy, using 100 c.c. of Hoechst's antistreptococcus serum, 50 c.c. the first day and as much the second day, injected in the gluteal region. If necessary he repeats these injections after five or six days, taking due precautions against possible anaphylaxis. The serum is polyvalent and

[3] **The New Medical Follies.** By Morris Fishbein, M.D., Editor of the Journal of the American Medical Ass'n and of Hygeia. Boni and Liveright, New York, 1927.

[4] **Biologie und Pathologie des Weibes.** Nos. 34, 35, 36, 37, 38, and 39. Edited by Halban and Seitz. Urban and Schwarzenberg, Berlin, 1927.

according to his experiences, of considerable value. He has also used rivanol intravenously with occasionally gratifying results. He is in favor of tying infected veins in cases of chronic thrombophlebitis, According to the literature quoted, 50 per cent of the patients recover. In puerperal peritonitis he inserts multiple drainage tubes and leaves ether in the peritoneal cavity before closure.

Freund discusses rupture of the uterus. Hammerschlag deals with trauma and operations during pregnancy, including external traumata, the effect of radium and x-ray. Sudden death in pregnancy, in labor and in the puerperium is described by Knauer.

Installment 35 contains an article by Guggisberg on the complications of pregnancy, labor and the puerperium due to disturbances resulting from the soft parts. Statistics show that very young primiparae have a shorter labor, less morbidity and mortality, and fewer tears than older ones. He considers that this applies up to the age of twenty-five years. In older women there is an increase in the duration of labor, weak pains are more frequent, and operative interventions are more often called for.

The same installment contains the beginning of the article on hydatid mole and malignant chorioepithelioma by Hitschmann. No new light has been thrown on the etiology of malignant chorioepithelioma up to the present day. He reviews all the older and modern theories. At present over 1000 cases are on record. He accepts no morphologic criteria as of value in forming a prognosis. If no metastases have occurred within the first two years after operation, the case may be considered cured. The extensive literature still confirms the present view of the great variability in malignancy of this type of tumor, some cases showing a benign course, others a regression after incomplete removal, still others proving rapidly fatal.

Installment 36 contains an extremely important and up-to-date monograph by Latzko and Schiffmann on the diseases of the genitourinary tract in the female and its relations to the female genital organs. The authors speak of Stoekel and Kolischer as the founders of gynecologic urology, apparently forgetting the many fundamental contributions of Howard Kelly. They condemn the use of the Pawlik-Kelly technic entirely, comparing the use of this technic to a hobby-horse in comparison to a live steed. Here again they forget that before the Nitze technic had been developed we were compelled, in default of other, to use endoscopic methods and that even today occasions arise when this simple and direct technic is of great aid.

They prefer indigocarmine to phenolsulphonephthalein for determining the excretory power of the kidney. They agree that the Ambard constant is not reliable, and they accord no value to the phloridzin method. They warn us that carcinoma of the urethra sometimes masks under the guise of an innocent caruncle. Although many methods are described, Coffey's method of implanting the ureters into the lower portion of the large bowel is favored above all others in the treatment of extrophy of the bladder. They see no difference between "the elusive ulcer" of Hunner and simple ulcer of the bladder. Furthermore they do not accept a metastatic origin of ureter stricture, resulting from tonsils and other distant sites of infection. They believe that the constant finding of ureter strictures is really due to local and transitory spasm. Little value is ascribed to neph-

ropexy. This monograph is carefully prepared, is well condensed, conservative, takes due consideration of the literature and may generally be summed up as sound and sane.

Installment 37 contains a short chapter on asepsis, including the preparation for labor and for operative interventions by Stickel. The author prefers ether. The chapter is short and colorless.

The next two treatises cover the physiology and pathology of the newborn, Reuss giving a short and comprehensive description, illustrated by many beautifully colored plates, as well as by numerous photographs.

Installment 38 deals with the biology and pathology of pregnancy and labor in domestic mammals. The contents will be of interest not only to obstetricians and gynecologists but also to biologists and investigators. Keller, among other topics, takes up the duration of pregnancy in various species, and their number of young. The methods of diagnosing pregnancy in animals is gone into, varying from abdominal examination in the smaller mammals, as well as the changes in the genitals and breasts, to vaginal and rectal palpation in the larger types, such as the cow and the mare. As in human medicine, biologic methods of diagnosing pregnancy have proved of no practical value, although many are instanced.

Much of interest is found in the description of labor and the puerperium, and in the various methods which animals employ or nature has devised in severing the cord postpartum. Umbilical infections are apparently not uncommon in animals and therefore are of economic importance. Vaginal prolapse occurs in a number of forms, particularly in the cow, mare and sheep. Extrauterine pregnancy is almost unknown and, on the whole, appears never to have been convincingly demonstrated except in the human being. Bacterial abortion is frequent. The author apparently agrees with some of our American veterinary obstetricians who believe that many other organisms besides the bacillus abortus of Bang are at fault. Distocia is taken up in detail as well as operative obstetrics.

Installment 39 deals with two aspects of carcinoma of the cervix. Kermauner describes the clinical aspects and operative treatment of carcinoma of the uterus. In conformity with other authors he divides the subject into corpus and cervix carcinomas, but acknowledges that in advanced conditions the original point of the origin cannot be determined. He sees no reason for further subdivision into portio and canal tumors. The etiology is as unclear as ever, such conditions as psychical state, race and social condition playing no definite rôle. Any etiologic value ascribed to these rests merely on the general impressions of various authors. The description, in many ways, follows that of the well-known book by Schottländer and Kermauner. Statistics show no increase of growth or increased malignancy during pregnancy. Much importance is ascribed to diagnostic excisions. No value is attached to a so-called malignancy index, the histology not aiding in predicting the future course. The many statistics are so confusing that they prove un-understandable to me. In operation he prefers the abdominal route. Apparently he subjects all cases in which the technical difficulties are not too great, to operative surgery.

Eymer, on the other hand, describes radium and x-ray treatment of

carcinoma of the cervix. The results with corpus carcinoma have been very poor. However, those with cervical carcinoma are encouraging, thus further justifying the stand of those of us who have abandoned the Wertheim operation in cancer of the cervix in favor of combined radio and x-ray therapy.

C. Jeff Miller has written a short *Outline of Gynecology for Students*[5] which deserves wider publicity than its modest format and its limited scope of circulation give to it. Based on his experience as a teacher, Miller has felt that the overburdened and overworked medical student deserves a carefully worked out but short exposition, which avoids the faults of the so-called syllabus and yet saves the student from wading through the many diffuse pages of the average textbook. The entire subject of gynecology is covered in a compass of 268 pages. This enables the third year student to actually study this text with some likelihood of remembering what he has read.

R. Franz has published a textbook for students and physicians on *Gonorrhea in the Female*.[6] This is a very comprehensive, short book, well planned out and covering the field most completely. The main objection to the text is that the author has not emphasized sufficiently those methods which have given him the best results and presents all the current methods of treatment without sufficient comment. Any one with experience will find it a most useful reference book, as every detail is carefully gone into. The culture methods recommended are not at all up to modern standards. The use of intrauterine injections is featured in the text, but the extreme dangers of this method are not sufficiently emphasized. The conservatism recommended during the acute stage of the disease or in the presence of peritoneal irritation is to be highly endorsed. On the whole Franz's is one of the most useful small textbooks on this subject existing in any language.

L'examen Médical en vue du Mariage[7] consists of a series of articles published under the auspices of the French Society of Eugenics with the aim of clarifying the opinion and knowledge of the public on the actual conditions of affairs. The ultimate aim is to modify the French marriage laws so as to have compulsory examination before marriage incorporated in them. Numerous well-known medical men and laymen have contributed. Legislation in the United States is freely quoted and every aspect of the subject discussed in detail, such as the general eugenic question, tuberculosis, venereal diseases, mental, and nervous diseases. It is encouraging that a strong movement dealing with this burning question is under way in various countries.

Evans, Burr, and Althausen have published a most thorough monograph on the *Antisterility Vitamine Fat Soluble E*[8] appearing in the *Memoirs of the University of California,* Volume VIII. This is a

[5] **An Outline of Gynecology for Students.** By C. Jeff Miller. Tulane University, New Orleans.

[6] **Die Gonorrhoe des Weibes. Ein Lehrbuch fuer Aerzte und Studierende.** By Dr. R. Franz. Verlag von Julius Springer, Wien, 1927.

[7] **L'examen Medical en vue du Mariage.** Ernest Flammarion, Editeur, Paris, 1927.

[8] **The Antisterility Vitamine Fat Soluble E.** By H. M. Evans and G. O. Burr. Memoirs of the University of California, Volume VIII. University of California Press, 1927.

worthy successor to Volume VI to which one of the authors (Long and Evans) contributed work on the Estrous Cycle in the Rat. The present monograph is based on an almost incredible amount of study and investigation.

The conclusion reached is that there is a substance present in the active fraction which is specific for curing a specific type of sterility induced by certain purified diets. "The cure has repeatedly been effected by as little as 5 mg. of concentrated fractions fed on the day of positive mating." Controls have never given litters. The vitamine appears to be a fat soluble material, biologically active and thermostabile. The authors compare the vitamine in many of its characteristics with the female sex hormone.

Sellheim[9] has written a short pamphlet on the treatment of sterility which appeared in the *Abhandlungen aus der Geburtshülfe und Gynäkologie und ihren Grenzgebieten.* Of the general causes he emphasizes sperma immunity, coitus abortus, previous appendicitis, as well as the regularly blamed conditions, such as sterility of the husband and impermeability of the tubes. He uses salpingography to determine the site of the stricture if present. He advises curettage in case of oldish patients recently married, as well as in patients who have used anticonceptional measures for a long time, without giving convincing reasons for this therapy. The monograph concludes with a description of numerous complicated technics for tubal implantation.

The second edition of Young's *Textbook of Gynecology*[10] (Edinburgh Medical Series) forms a short book for students. The text is concise, clear, and on the whole adequate and up to date. The illustrations are numerous, somewhat diagrammatic and in many instances the same cuts are repeated in different connections. The three types of pessaries advised (the spring core ring, the shelf pessary—a modified Zwank—and the cup and stem) are the very ones which I have found least useful and most dangerous.

Fischer's short monograph on the *Gynecology of Dioskurides and Plinius*[11] will prove of interest to the student of the history of medicine. Obstetrics is also discussed.

OBSTETRICS

Prof. George Winter has published an operative obstetrics,[12] the main portion of the text having appeared in Halban and Seitz's *Biology and Pathology of Women.* As this huge series of monographs is inaccessible to the average student and practitioner, he has thought it worth while to revise the text for their benefit and have it appear in the form of a single volume. Prof. Winter is ably assisted in his task by Benthin and Naujoks, who have written several of the chapters.

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[9] **Weitere Fortschritte der Sterilitaetsbehandlung.** By Hugo Sellheim. Verlag von S. Karger, Berlin, 1927.

[10] **A Textbook of Gynecology.** By James Young. Ed. 2. Macmillan Co., New York, 1927.

[11] **Die Gynaekologie bei Dioskurides und Plinius.** By I. Fischer. Julius Springer, Wien., 1927.

[12] **Lehrbuch der operativen Geburtshilfe fuer Aerzte und Studierende.** By Prof. Dr. Georg Winter. Urban and Schwarzenberg, Berlin, 1927.

Spinal anesthesia has been abandoned as being too dangerous. As is usual in Europe, the authors prefer chloroform for the induction of narcosis but, if prolonged anesthesia is necessary, switch over to ether. An extremely conservative attitude is observed toward the induction of abortion in the face of medical and other indications. The authors say that both for ethical and legal reasons the induction of abortion, from the eugenic standpoint, is not permissible. The eugenists, and here I feel that most medical men agree, believe that retinitis pigmentosa, amaurotic idiocy, dementia precox, genuine epilepsy, Huntington's chorea, maniac depressive insanity, degenerative hysteria, Pelizans-Merzbach disease, should really be accepted as indications. I notice with surprise that laminaria tents for dilatation are still recommended. Winter considers vaginal cesarean a valuable method but I note that in twenty years only 56 cases were treated by this technic at his clinic. Hebosteotomy is still practiced although from 3 to 10 per cent of bladder injuries occur. The Kielland forceps has been found useful with the head high up. This is a very complete and well-written textbook throughout, which, on the whole, conforms fairly closely with our American procedures.

Two monographs by Vignes[13] and Bach[14] are extracts from *Traité de Physiologie Normale et Pathologique*. The first, by Vignes alone, deals with the genital apparatus of the woman. It is encyclopedic in scope, exhaustive in treatment, with a minute scrutiny of the literature. References which I have been looking for in vain for years, I at last come across as footnotes. The subjects covered are the principal functions of the genital tract, including the menstrual cycle, the associated tracts and the effect of menstruation upon them, the theory of menstruation, the physiology of sex, and finally, deviations from the normal. This is a most valuable contribution because of its exhaustive treatment of the subject, its short compass, and its reference to original sources.

The second monograph in collaboration with E. Bach deals with the pregnant woman, pregnancy, embryo, fetus, and placenta. These subjects have been treated in an identical manner with equally happy results. Both monographs can be used as reliable sources of reference.

Heidler and Steinhardt have treated the subject of manual removal of the placenta.[15] Their material comprises 1000 cases obtained from a total material of 64,000 cases or 1.56 per cent. The general mortality is high, being 8.2 per cent throughout this period which covers twenty-one years. Two and eight-tenths per cent died of hemorrhage and 1 per cent of sepsis, the remaining being ascribable in most instances to the underlying diseases rather than to the method employed in delivering the placenta. The morbidity was 29.52 per cent altogether. I cannot refrain from forming the impression that, in conservative hands, manual removal of the placenta will always remain a rare intervention, because waiting so regularly proves suc-

[13] **L'Appareil Genital Femelle.** By H. Vignes.

[14] **La Femme Enceinte. La Gestation. L'Embryon et le Foetus. Le Placenta. Extrait du Traite de Physiologie Normale et Pathologique.** By H. Vignes et E. Bach. Publié sous la direction du Pr. G.-H. Roger. Secrétaire Général: Léon Binet. Vol. xi. Masson et Cie, 1927.

[15] **Ueber die Manuelle Plazentaloesung.** By Dr. H. Heidler and Dr. B. Steinhardt, von Curt Kabitzsch, Leipzig, 1927.

cessful, and because every effort should be made to keep out of the uterus in view of the danger of the procedure.

Ford, Crothers, and Putnam's book[16] is a part of a series of *Medicine Monographs*, each of them representing a comprehensive critical review of some important medical problem. Undeniably the question of injury of the child during birth is one of outstanding interest. Discussed in all its many aspects a few years ago by Ehrenfest, we find here a more detailed consideration solely of birth trauma of the central nervous system. Ford deals in the first part of the volume with cerebral injuries. After quoting the more or less known and accepted views concerning etiology and pathology, he discusses critically the intricate but yet most significant relation of such injuries to physical and mental development in later life. Most valuable excerpts of clinical histories are presented. The final conclusions drawn from this study are laudably conservative, at least in comparison with the noticeable trend of some recent writers, to ascribe almost all later deficiencies to cerebral birth traumatism.

In similar manner Crothers and Putnam in the second part of the volume deal with the injuries of the spinal cord. They fully confirm the view previously expressed by obstetricians that undue traction plays the significant etiologic rôle. Much of this knowledge we owe to the original investigations of Crothers. They come to the definite conclusion that traction on the spinal cord during birth produces cord injuries which represent a very important cause of physical disabilities noted in children.

Six authors have combined to write *The Queen Charlotte's Practice of Obstetrics*.[17] This volume was written to set forth the views held and the methods practiced by those at present connected with the staff of this hospital. The hospital is the earliest lying-in hospital in Britain. It has moved several times since its foundation and at present is apparently housed under modern conditions. From 1900 to the present time, approximately 1800 women were delivered in the hospital and 2100 in their homes each year.

The subjects covered are the usual ones, namely, development and anatomy, normal and abnormal pregnancy, labor and puerperium. There follow sections on the baby, on obstetric operations and the concluding section on miscellaneous subjects which embrace such varied topics as insanity, pituitary extract, anesthesia, x-ray, vaccination and statistics covering Great Britain and continental Europe, maternal and fetal mortality. On the whole the volume does not make an exceptionally favorable impression. A fairly active interference in abortion, including curettage if the products of conception are not expelled within twelve hours, does not conform with modern American practice. In the treatment of vomiting and toxemia of pregnancy no mention is made of the modern method of giving glucose by rectum or vein, or the treatment by glucose and insulin combined. In eclampsia no mention of the Stroganoff method is made.

[16] **Birth Injuries of the Central Nervous System.** By Frank Ford, Bronson Crothers, and Marian C. Putnam. The Williams and Wilkins Co., Baltimore, 1927.

[17] **The Queen Charlotte's Practice of Obstetrics.** By J. B. Banister, A. W. Bourne, T. B. Davies, L. C. Rivett, L. G. Phillips, and C. S. Lane-Roberts. Wm. Wood and Co., New York, 1927.

On the whole this book has little to recommend it although it is well gotten up and adequately illustrated.

Kupferberg[18] has edited live topics in obstetrics appearing in the series of the *Kleine Klinische Bücherei*, No. 25. Because of the marked reduction of the birth rate, he emphasizes the necessity of conserving both maternal and fetal life and health, dealing exclusively with serious complications. Most of these articles have appeared previously either in *Medizinische Klinik* or *Der Praktische Arzt*. Such subjects as amelioration of pain during labor, oxytoxics, and drugs favoring uterine contraction, conduct of labor without vaginal examination, etc., are dealt with.

The third edition of Maygrier and Schwaab's *Précis d'Obstétrique*[19] is a thick volume of over 1200 pages, which deals with the subject in the accepted fashion. The illustrations which depict obstetric procedures with the ungloved hand, and occasionally with starched cuffs unremoved, are, I confess, somewhat disturbing.

ENDOCRINOLOGY

A number of installments of the *Handbuch der Inneren Sekretion*[20] have been received. They are issued irrespective of their sequence, which can be done without disturbance because of the fact that each contribution represents a separate monograph.

Volume I, Installment 3, by Berberich and Fischer-Wasels, deals with the thyroid and internal secretions. The authors point out that the thyroid, parathyroid, and thymus are all three of branchial derivation. The thyroid gland undergoes transitory and usually symptomless changes in acute and chronic infections. In the latter class of cases, symptoms may, however, develop. Physiologically the thyroid appears to increase at the time of puberty, premenstrually, and in pregnancy. If the thyroid is absent or diseased, the chief cells of the hypophysis increase, as well as the colloid they store. The connective tissue of the hypophysis likewise increases under these conditions and dilatation of the capillaries may occur. Being of conservative trend, the authors refuse to commit themselves as to whether these two glands of secretion are antagonists or synergists. In all the so-called pluriglandular syndromes, the thyroid is also affected. The effect of thyroid changes on the skin, muscle, bone and nervous systems are discussed in detail.

The division of struma into the nodular and diffuse type is accepted, but many transitional forms occur. Struma diffusa parenchymatosa most often is accompanied by Basedow symptoms. This change is rarely found without the occurrence of exophthalmic goiter. Most characteristic is the increase in size of the cells of the follicle epithelium, the colloid contents of the acini being diminished, and the colloid appearing more fluid. Diffuse colloid struma may be found with perfectly normal function or accompanied by either in-

[18] **Geburtshilfliche Tagesfragen.** Edited by Med.-Rat Dr. Kupferberg. Repertorienverlag, Leipzig, 1925.

[19] **Precis d'Obstetrique.** Ed. 3. By C. Maygrier and A. Schwaab. Collection Testut. Gaston Doin and Cie, Paris.

[20] **Handbuch der Inneren Sekretion.** Vol. I, No. 3; Vol. II, No. 3; Vol. III, Nos. 2 and 3. By Dr. Max Hirsch. von Curt Kabitzsch, Leipzig.

crease or decrease of function. Struma nodosa (adenoma) is described, but the authors do not believe in its fetal origin.

The same authors describe the parathyroid. They go into the morphology and the changes in morphology in disease. They confess that our knowledge of this gland is still somewhat vague. I find not a single reference to Collip's work in their discussion except the paragraph, "The therapeutic results obtained by recent American authors with parathyroid extract in tetany are to be utilized in the same sense" (as parathyroid transplants in tetany).

The physiology of the thymus is discussed by Thomas. Nothing is known about thymus secretion. There are a few facts favoring a theory of a growth hormone. The effect on metabolism is nil. The extreme and rapid atrophy of the thymus in starvation is striking. A lympho-stimulating function is fairly certain, causing an increase and outpouring into the blood stream of lymphocytes.

A nearly 400-page article on the adrenals has been contributed by Bayer. As all previous authors, he divides the gland into chromaffin and cortical portion which are separately discussed. He is by no means certain that the chromaffin tissue is necessary for the continuance of life. Certain stimuli increase the adrenal secretion. Innumerable stimuli are discussed including drugs, chemicals and organ extracts. The pharmacology of adrenalin secretion, especially the effects on various parts of the circulation, the mucosae, organs and secretions are entered into in great detail as well as the discussion of the toxicology of this drug.

Death follows from complete removal of the cortex with constant, complete absence of the liver glycogen. There may be an effect on the vitamine metabolism. The question of a possible detoxifying rôle of the adrenals shows how little we know of this organ. Its influence on cholesterol, on pigmentation, on cholin production are all taken up, as well as the subject of hyperadrenalism. The adrenals, as is well known, regularly increase during pregnancy. A possible relation between the cortex and medulla has to be considered. This section is very detailed, very instructive, but would have been even more so if the author, whose experience in this field is extensive, had drawn his own deductions for the benefit of the readers and had summarized to a greater extent than he has.

A short chapter on the parotid, stomach, intestine, liver, and spleen is supplied by Zuelzer. He considers that the most important work on liver function has been contributed by Mann and Magath by their studies made after complete hepatectomy. This appears to show that grape sugar is really the liver hormone. Adrenalin mobilizes the glycogen in the liver. The gastric secretion may possibly be cholin. He believes that the parotid secretes a hormone antagonistic to adrenalin.

In Volume III, Installment 2, Josefson has described the clinical manifestation of hypophyseal disturbances. He gives a good clinical description of hypo- and hyperfunctional conditions. Evidently he does not believe in the efficacy of any hypophyseal extracts, nor does he ascribe any value to them in the treatment of hypofunction.

Aschner, who deals with the clinical manifestation of the epiphysis, on the other hand, shows marked credulity as to the effect of organotherapy. The epiphysis does not involute at the age of

seven years; it is effected by castration and pregnancy in both its size and shape. Epiphyseal disturbances manifest themselves by premature development, adiposity, and psychic disturbances.

Diseases of the thymus by Thomas. In this installment the author considers the thymus as a multiplicator of the thyroid in Basedow. In the course of other endocrine diseases there may be thymus stimulation or, what shows clinically in the same fashion, a removal of thymus inhibition with consequent lymphocytosis, but throughout the thymus plays the subsidiary rôle.

The clinical pathology of the adrenals is taken up by Ehrmann and Dinkin. The best known syndrome is that of Addison which is a hypofunctional condition, manifesting both acute and chronic types, the latter with pluriglandular changes. Temporary Addisonian symptoms are common after infectious diseases, avitaminoses, rachitis and pregnancy. No definite proof has ever been offered of adrenalin reduction in the blood of Addison's disease. Adrenal therapy is rarely a success and if attempted, the fresh gland should be employed. The article contains much loose reasoning on the hypofunction of the medulla. The clinical reports on virilistic changes in females consequent to hypertrophy of the cortex are brought thoroughly up to date.

The longest chapters in this installment deal with the clinical pathology of the female sex glands as related to endocrine disturbances. These chapters should be considered more the expressions of opinion and the experiences obtained at the clinic of Prof. L. Fraenkel of Breslau than the fully accepted views now current. These chapters fill 200 pages. The subject is much complicated by the supposed interaction of various glands but for the sake of simplicity, has been divided into (1) disturbances of development, (2) functional changes, (3) pregnancy changes, (4) mammary influence, (5) tumors.

Herschan deals with developmental disturbances including precocious puberty, late menstruation, puberty bleeding, infantilism, asthenia, eunuchoidism, and hermaphroditism. To Geller was assigned functional disturbances. He considers every disturbance of cycle as hypo- or disfunctional and never as hyperfunctional. Just why he arrives at this conclusion, after the fairly definite evidence that my associates and I have offered on the blood findings, is not quite clear to me. He correctly concludes that histologic examinations will never solve the question and likewise that the *present* ovarian therapy does not substitute for lack of ovarian activity. Among the subjects taken up are ovarian sterility, fluor, general disturbances outside the genital system, climax and castration.

Hermstein deals with the breast. I notice that he still accepts Clayton and Starling's theory on the effect of fetal extracts on the breasts although this work has been repeatedly proved fallacious. Fraenkel himself deals with tumors of the endocrine glands in their relation to the genital system. This is a well written and interesting chapter which, however, is unconvincing because of the many gaps still existing in our knowledge.

The final installment in this series received is Volume III, Number 3, containing an article on cachexia strumipriva by Klose and Büttner. They discuss the history, the effects on adult and child, and the report made by Kocher in 1906 on 38 cases of total thy-

roidectomy. Of these, 26 per cent died, the average course being seven years. An interesting exposition of the effect of thyroidectomy on various species of animals is given. Myxedema following x-ray, the larvated or forme fruste are gone into. The authors seem to feel that thyroid medication does not always or entirely replace complete thyroidectomy.

The beginning of the long and complete monograph on goiter and cretinism by Eggénberger completes this installment. He enters into the distribution in endemic regions and into the interesting geographical variations. Careful details of how to measure the thyroid in the living are given. He estimates that in the entire world there are at least 15 million persons who show visible enlargement of the thyroid. Many good illustrations illuminate the text. The author believes that a morphologic-functional classification is impossible. Marine in 1907 first showed that endemic goiter was a deficiency disease and due to some chronic dietary deficiency. The thyroid evidently hypertrophies to obtain enough iodine from the diminished concentration found in the circulation. He describes in detail the until recently puzzling endemic areas often adjacent or surrounded by other areas relatively free of the disease. It was finally discovered that the source of salt in these endemic areas was different from that of adjacent cantons and due to the lack of iodine in the salt supply. In Switzerland iodine prophylaxis has been taken up by the government and has gradually become widespread. This article is particularly well planned and well carried out.

Recent progress in endocrine therapy as viewed by collaboration of numerous authors has just appeared.[21] The text is in the form of twelve lectures, the first by Prof. Carnot which deals with the general subject, such as implantations and transfusions of blood as a means of endocrine therapy. Weil prefers the citrate method of transfusion. Gley doubts that thyroxin is a fully purified hormone and suggest the hypothesis of several thyroid substances. Binet discusses the hypophysis. Baudouin, in my opinion, prematurely speaks of the use of an active anterior lobe extract. At the moment I know of no such active substances obtainable for therapeutic purposes. Pézard has an excellent article on the physiology of the male gonads. Vignes has an equally good discussion pertaining to the female gonads. He takes a commendably conservative stand on all the therapy. His optimism in regard to mammary gland extract seems unjustified to me.

In summing up this very valuable contribution, it appears that the exposition of the physiologic topics throughout has been sane, conservative and good, but that the authors unconsciously yielded to the pressure brought by the entire medical profession in their eager demand for effective endocrine preparations. The authors have been somewhat too optimistic in their conclusions on opotherapy.

MISCELLANEOUS

Royster has written on appendicitis,[22] appearing in the *Surgical Monographs* edited by Dean Lewis, Eugene H. Pool, and Arthur W.

[21] **Les Progres Recents en Therapie Endocrinienne.** By P. Carnot, P. E. Weil, E. Gley, P. Harvier, L. Binet, A. Baudouin, L. Hallion, F. Rathery, A. Pézard, H. Vignes, R. Gayet, and E. Gergen, J. B. Baillière et Fils, 1927.

[22] **Appendicitis.** By H. A. Royster, M.D. D. Appleton and Co., New York, 1927.

Elting. This monograph is gotten up in extremely attractive form and covers the subject in great detail. The author has accepted Fowler's classification of endo-, parietal-, peri-, and para-appendicitis, which, however, is purely descriptive, and then gives a second or clinical classification containing eight varieties. It appears to me that it would be better to adopt a classification such as that offered by Moschcowitz which conforms both to pathologic criteria and clinical needs. In the matter of diagnosis Royster believes that right salpingitis can more readily be excluded than has been my experience. He then quotes Ten Berge who in 24 cases made 3 wrong diagnoses, an incidence of error of 12 per cent! Metastatic carcinoma of the appendix deserves some mention although a very rare disease. He favors gridiron and right rectus incisions. The author apparently also prefers burying of the stump to simple ligation. All in all this monograph is both readable and instructive.

The second volume of *Operations of Surgery* by Rowland and Turner[23] is a profusely and adequately illustrated volume of nearly 900 pages. The subject covered in Volume II is the entire abdomen. The text is extremely detailed and carefully worked out. The world's literature is minutely gone into with references as footnotes, covering the entire world. American sources are given full credit. Operative indications are considered in each instance and the results of operations are likewise recorded. Both the male and female genital systems are included.

The book should prove a valuable guide not only to operative technic but also as a reference volume for looking up the literature.

Preoperative, operative and postoperative surgical technic, including the principles of anesthesia, asepsis and wound treatment are dealt with by Paul Zander[24] and his collaborators in a series of small booklets called *Kleine Klinische Bücherei*, Installment 28. The editor says that since the war, country doctors are operating more than previously. This book is designed for them as well as for the younger hospital assistants. The monograph, in addition, contains chapters on the treatment of furuncles, finger injuries, and infectious diseases of the physician. Numerous subjects are covered, such as indications, amelioration of pain, prevention of wound infections. Ether is preferred over other anesthetics, quite a new stand for central European authors to take. For skin disinfection 5 per cent iodine, 75 per cent alcoholic tannin solution, or 5 per cent thymol alcohol are advised, all of which disinfectants act similarly by shrinking and tanning the skin.

The *Textbook of Topographic Anatomy* by Blumberg[25] is written for the benefit chiefly of students, with the view of connecting their purely theoretic anatomic studies with clinical medicine and surgery. The author, until his retirement from active practice, was a surgeon and therefore fully appreciates the practical side of applied anatomy. The numerous and striking illustrations, whenever possible, are drawn from the right side of the body in order to facilitate orienta-

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[23]**The Operations of Surgery.** By R. P. Rowlands, O.B.E., and P. Turner, B.Sc. Ed. 7, Volume II, The Abdomen. Macmillan Co., New York, 1927.

[24]**Vorbereitung, Durchfuehrung, Nachbehandlung chirurgischer Eingriffe Grundsaetze der Schmerzbetaeubung, Aseptik, Wundversorgung. Aus der Praxis fuer die Praxis.** By Prof. Dr. P. Zander. Repertorienverlag, Leipzig, 1926.

[25]**Lehrbuch der Topographischen Anatomie.** By J. Blumberg. Urban and Schwarzenberg, Berlin, 1926.

tion. Of the 152 chiefly multicolored illustrations all but 9 are original. The book makes an excellent impression, the text being simple and clearcut. As an example of how carefully clinical points are kept in view, I may instance that both the lateral and posterior regions of the ribs are depicted and discussed in order to show that the needle, in aspiration of the pleura must be inserted close to the upper border of the lower rib posteriorly, while laterally the site of puncture should be equidistant from the two ribs. Even the female genital tract, which so often in books of this nature is most scantily dealt with, receives adequate treatment.

Keiller's *Nerve Tracts of the Brain and Cord*[26] is a short, well-planned book for students, which emphasizes particularly the anatomy, physiology, and pathology as an introduction to neurology.

Part I is designed to be used as a laboratory manual, for both normal and pathologic neurology. Part II applies these anatomic descriptions to the physiology, while Part III describes the clinical syndromes in a very clear-cut fashion. The illustrations are numerous but extremely crude, yet, although offending the artistic sense, they really illustrate the text convincingly.

International Clinics, Volume II, Series 37,[27] contains numerous articles of which none happen to be of particular interest to our readers with the exception of the rules for operation at the clinic for obstetrics and gynecology of the University of Florence.

The last number of *International Clinics,* Volume III, Series 37, 1927,[28] contains a number of interesting articles. One of the most stimulating is that of Theobald Smith on the *Passing of Disease from One Generation to Another and the Processes Tending to Counteract It.* The most striking examples are those of the chrysalis of the silkworm and ovum of the tick infected with Texas fever, in which the parasites are directly transferred by means of the infected ovum. He takes up malarial infestation of children in Africa, as well as tuberculosis and syphilis in the human being. The efforts to counteract and protect are well-evidenced by the antibodies obtained in milk. An interesting experiment is being conducted on a very small flock of sheep in whom successive generations of lambs have been repeatedly isolated and the parasitic infestation has been reduced to a minimum.

The article of T. R. Brown on *Colitis* is well worth reading, and that of C. E. Simon on the *Virus of Herpes Simplex* is of great importance. W. F. Harriman discusses the indications and contraindications of the Kielland forceps which he favors particularly when the head is in the transverse diameter.

How to Make Periodic Health Examinations by Fisk and Crawford[29] is a manual of procedure. The book is launched with a foreword by Major General Ireland and by introductions to each chapter by an imposing list of authorities no less than sixteen in number. Every

[26] **Nerve Tracts of the Brain and Cord. Anatomy: Physiology: Applied Neurology.** By Wm. Keiller, F.R.C.S. Macmillan Co., New York, 1927.

[27] **International Clinics. Volume II; Series 37. J. B. Lippincott Co., Philadelphia, 1927.**

[28] **International Clinics. Volume III; Series 37. J. B. Lippincott Co., Philadelphia, 1927.**

[29] **How to Make Periodic Health Examinations.** By E. Fisk and J. Crawford. Macmillan Co., New York, 1927.

portion of the human body is considered, also laboratory standards as well as methods of counselling. The book should prove a useful guide.

Bainbridge's book on *The Problem of Cancer*[30] is here presented in an Italian translation by Perilli and Pozzi with a preface by Alessandri. A very striking full-page photograph of the author, in uniform, forms the second frontispiece.

[30] **Il Problema del Cancro.** By W. S. Bainbridge. Luigi Pozzi, Rome, 1927.

Morris: On the Causes and Prevention of Maternal Morbidity and Mortality. Medical Journal of Australia, 1925, ii, 301.

While the death rate from general causes has been declining, the puerperal mortality rate has been rising. The puerperal mortality rate is excessive and is capable of being reduced. Though actual statistics of maternal morbidity are not available, there is little doubt that the total maternal morbidity exceeds by far the mortality resulting from pregnancy and childbirth.

Maternal mortality, and especially maternal morbidity, varies in direct proportion to the inefficiency or inadequacy of the professional care and supervision during the antenatal, natal, and postnatal periods.

The midwife's responsibility in the causation of maternal mortality is not as great as is customarily held; the medical profession must, individually and collectively, assume a larger share of such responsibility than has prevailed in the past.

Artificial abortion probably plays an important part in the production of maternal morbidity and mortality. Venereal disease, especially gonorrhea, is a potent factor.

Employment of women in Australia does not appear to have any marked effect on their maternal welfare. Insanitary conditions in the home have, apparently, little influence, at least on normal labors, though they probably increase the danger in those cases involving operative interference. The control of puerperal sepsis as a cause of maternal mortality in private practice has not been commensurate with that effected in public hospitals.

Operative procedures, especially delivery by forceps, are too frequently employed and leave in their wake a certain proportion of mortality and a far greater amount of morbidity and ill health.

Antenatal care and supervision afford a means of controlling much of the present maternal mortality and of eliminating most of the maternal morbidity. Its value is not fully recognized and, until it is, we shall not make any marked advance from the present unsatisfactory position. NORMAN F. MILLER.

Item

The Fifty-third Annual Meeting of the American Gynecological Society will be held at the Mayflower Hotel, Washington, D. C., on April 30, May 1 and 2, 1928.

Books Received

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VORBEREITUNG UND NACHBEHANDLUNG CHIRURGISCHER EINGRIFFE. Von Professor Dr. Paul Zander, in Darmstadt. Repertorienverlag in Leipzig, 1926.

BIOLOGIE UND PATHOLOGIE DES WEIBES. Herausgegeben von Halban und Seitz. Lieferungen 38 and 39. Verlag von Urban & Schwarzenberg, Wein, 1927.

LEHRBUCH DER OPERATIVEN GEBURTSHILFE. Von Professor Dr. Georg Winter, Universitaets-Frauenklinik in Koenigsberg, unter Mitwirkung von Professor Dr. W. Benthin und Dozent Dr. H. Naujoks. Mit 228 zum Teil farbigen Abbildungen in Text und 11 Tafeln. Verlag von Urban & Schwarzenberg, Wien, 1927.

HANDBUCH DER INNEREN SEKRETION. Herausgegeben von Dr. Max Hirsch in Berlin. II. Band, Lief. 3. Verlag von Curt Kabitzsch, Leipzig, 1927.

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APPENDICITIS. By Hubert Ashley Royster, Raleigh, N. C. D. Appleton & Company, New York, 1927.

NERVE TRACTS OF THE BRAIN AND CORD. By William Keiller, professor of anatomy, University of Texas. The Macmillan Co., New York, 1927.

THE ANTISTERILITY VITAMINE FAT SOLUBLE E. By Herbert McLean Evans and George O. Burr. University of California Press, Berkeley, Cal., 1927.

DER KALKBEDARF VON MENSCH UND TIER. Von Dr. Oscar Loew. Verlag Otto Gmelin, Muenchen, 1927.

FRUEHENTWICKLUNG, EIHAUTBILDUNG UND PLACENTATION. Von Professor Otto Grosser, an der deutschen Universitaet in Prag. Mit 297 abbildungen im Text. Verlag von J. F. Bergmann, Muenchen, 1927.

CONVALESCENCE, HISTORICAL AND PRACTICAL. By Dr. John Bryant. The Sturgis Fund of the Burke Foundation, New York, 1927.

METHODS AND PROBLEMS OF MEDICAL EDUCATION. Eighth Series. Rockefeller Foundation, New York, 1927.

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ANNUAL REPORT OF THE SURGEON GENERAL OF THE PUBLIC HEALTH SERVICE OF THE UNITED STATES. For the fiscal year 1927. Government Printing Press, Washington, 1927.